



US009440016B2

(12) **United States Patent**
Lin et al.

(10) **Patent No.:** **US 9,440,016 B2**
(45) **Date of Patent:** ***Sep. 13, 2016**

(54) **HEMODIALYSIS AND PERITONEAL DIALYSIS SYSTEMS HAVING ELECTRODIALYSIS AND ELECTRODEIONIZATION CAPABILITIES**

(51) **Int. Cl.**
A61M 1/16 (2006.01)
A61M 1/28 (2006.01)
(Continued)

(71) Applicants: **Baxter International Inc.**, Deerfield, IL (US); **Baxter Healthcare S.A.**, Glattpark (Opfikon) (CH)

(52) **U.S. Cl.**
CPC *A61M 1/1696* (2013.01); *A61M 1/1674* (2014.02); *A61M 1/28* (2013.01);
(Continued)

(72) Inventors: **Rongsheng Lin**, Buffalo Grove, IL (US); **Yuanpang Samuel Ding**, Libertyville, IL (US); **James M. White**, Grayslake, IL (US); **Ye Chen**, Buffalo Grove, IL (US); **Ying-Cheng Lo**, Green Oak, IL (US); **Joshua Miller**, Wilmette, IL (US); **Justin Rohde**, Des Plaines, IL (US)

(58) **Field of Classification Search**
CPC *A61M 1/1674*; *A61M 1/1696*; *A61M 1/287*; *A61M 1/28*; *B01D 61/243*; *B01D 61/44*; *B01D 61/58*; *B01D 61/422*
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

(73) Assignees: **Baxter International Inc.**, Deerfield, IL (US); **Baxter Healthcare S.A.**, Glattpark (Opfikon) (CH)

3,617,545 A 11/1971 DuBois et al.
5,244,568 A 9/1993 Lindsay et al.
(Continued)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

FOREIGN PATENT DOCUMENTS

WO 03/040042 5/2003
WO 2010/024963 3/2010

OTHER PUBLICATIONS

(21) Appl. No.: **14/684,675**

International Search Report for International Application No. PCT/US2010/026336, mailed Jul. 26, 2010.

(22) Filed: **Apr. 13, 2015**

(Continued)

(65) **Prior Publication Data**

US 2015/0209500 A1 Jul. 30, 2015

Primary Examiner — John Kim

(74) *Attorney, Agent, or Firm* — K&L Gates LLP

(57) **ABSTRACT**

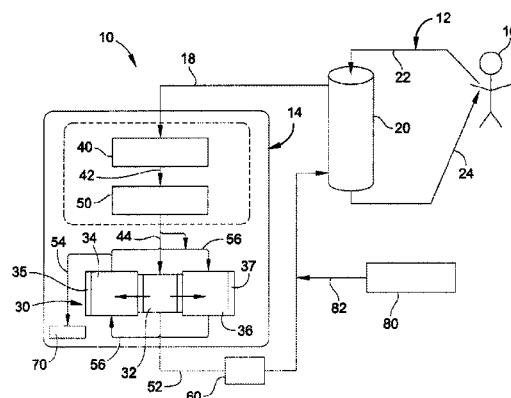
Systems and methods for hemodialysis or peritoneal dialysis having integrated electrodialysis and electrodeionization capabilities are provided. In an embodiment, the dialysis system includes a carbon source, a urease source, an ED/EDI unit. The carbon source, urease source, and/or the ED/EDI unit can be in the form of removable cartridges.

Related U.S. Application Data

(63) Continuation of application No. 13/796,799, filed on Mar. 12, 2013, now Pat. No. 9,005,440, which is a continuation-in-part of application No. 12/718,609, filed on Mar. 5, 2010, now Pat. No. 8,858,792.

(60) Provisional application No. 61/158,101, filed on Mar. 6, 2009.

10 Claims, 15 Drawing Sheets



- | | | |
|------|---|--|
| (51) | Int. Cl.
B01D 61/24 (2006.01)
B01D 61/42 (2006.01)
B01D 61/44 (2006.01)
B01D 61/58 (2006.01) | 7,318,892 B2 1/2008 Connell et al.
2003/0105424 A1 6/2003 Karoor et al.
2007/0179431 A1 8/2007 Roberts et al.
2008/0164209 A1 7/2008 Zacerkowny et al.
2010/0224492 A1 9/2010 Ding et al.
2012/0273354 A1 11/2012 Orhan et al.
2013/0186759 A1 7/2013 Lin et al. |
|------|---|--|

- (52) **U.S. Cl.**
 CPC *A61M 1/287* (2013.01); *B01D 61/243* (2013.01); *B01D 61/422* (2013.01); *B01D 61/44* (2013.01); *B01D 61/58* (2013.01)

OTHER PUBLICATIONS

- (56) **References Cited**

U.S. PATENT DOCUMENTS

5,350,357 A	9/1994	Kamen et al.
5,585,003 A	12/1996	Van Newenhizen
5,662,806 A	9/1997	Keshaviah et al.
5,873,853 A	2/1999	Keilman et al.
5,984,891 A	11/1999	Keilman et al.
6,187,162 B1	2/2001	Mir
6,196,992 B1	3/2001	Keilman et al.
6,592,542 B2	7/2003	Childers et al.

International Preliminary Report on Patentability for International Application No. PCT/US2010/026336, mailed Aug. 5, 2011.
 International Search Report for International Application No. PCT/US2014/016376, dated May 22, 2014.
 Manns et al., "The acu-men™: A new device for continuous renal replacement therapy in acute renal failure," *Kidney International*, 1998, vol. 54, pp. 268-274.
 Written Opinion for International Application No. PCT/US2010/026336, mailed Jul. 26, 2010.
 Written Opinion for International Application No. PCT/US2014/016376, dated May 22, 2014.
 Canadian Office Action dated Feb. 16, 2016, corresponding to Canadian Patent Application No. 2,754,522. 4 pages.

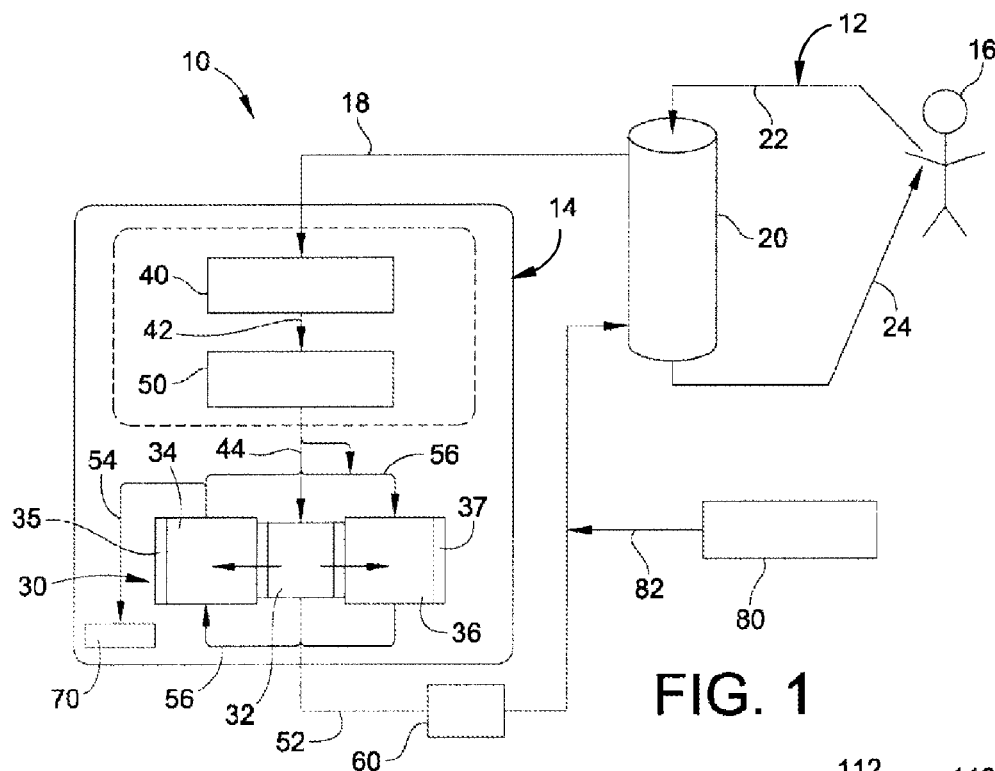


FIG. 1

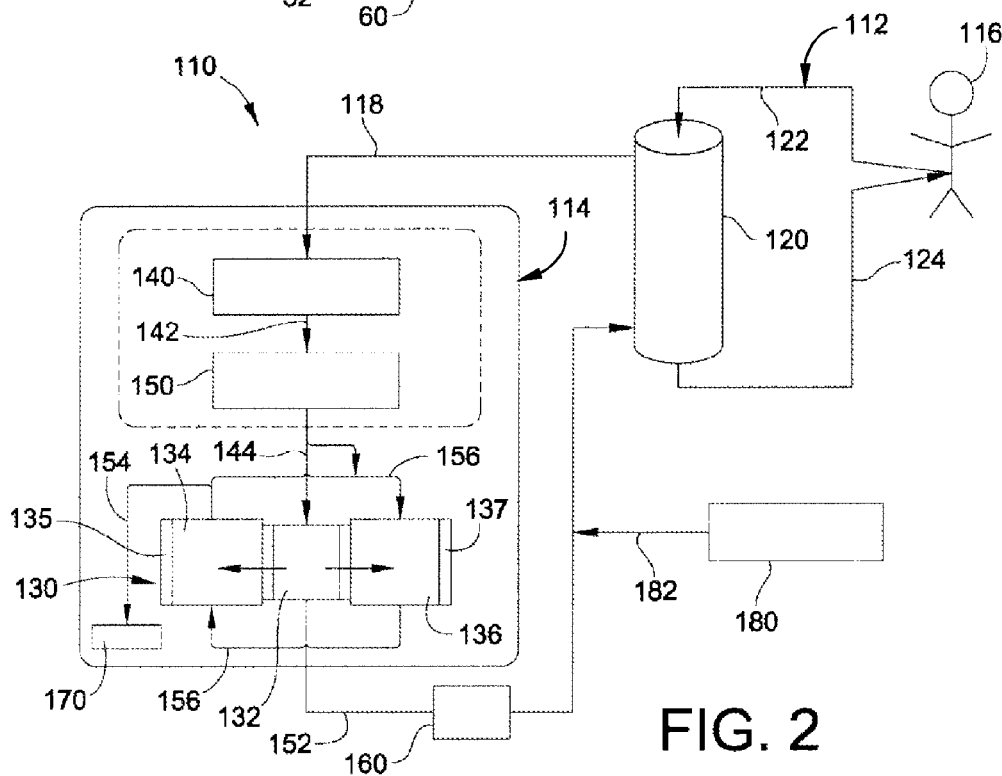
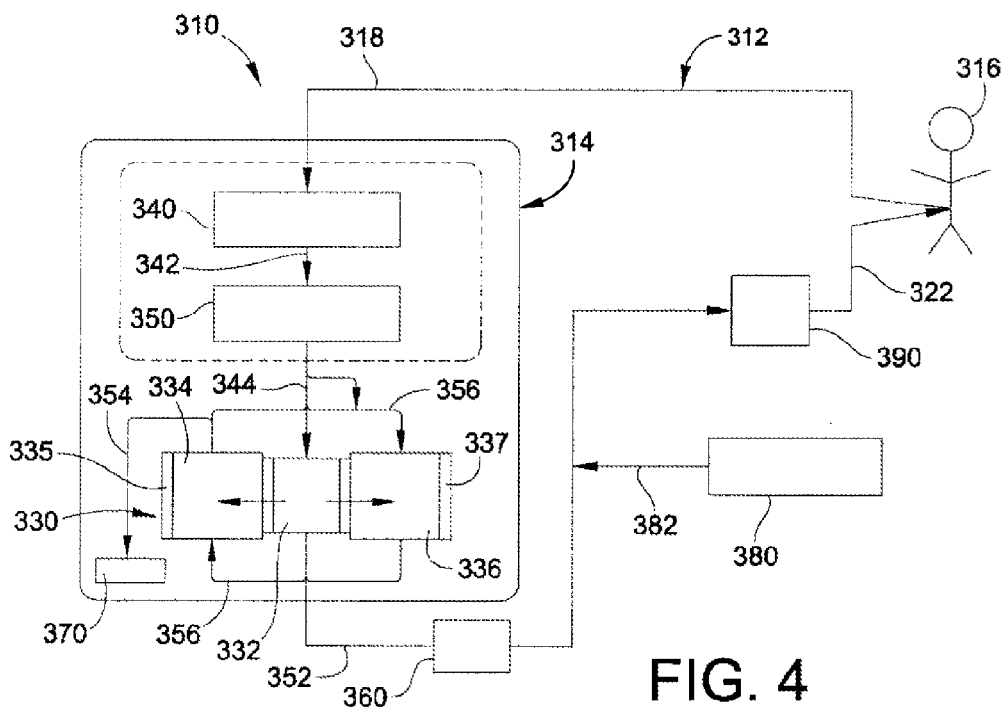
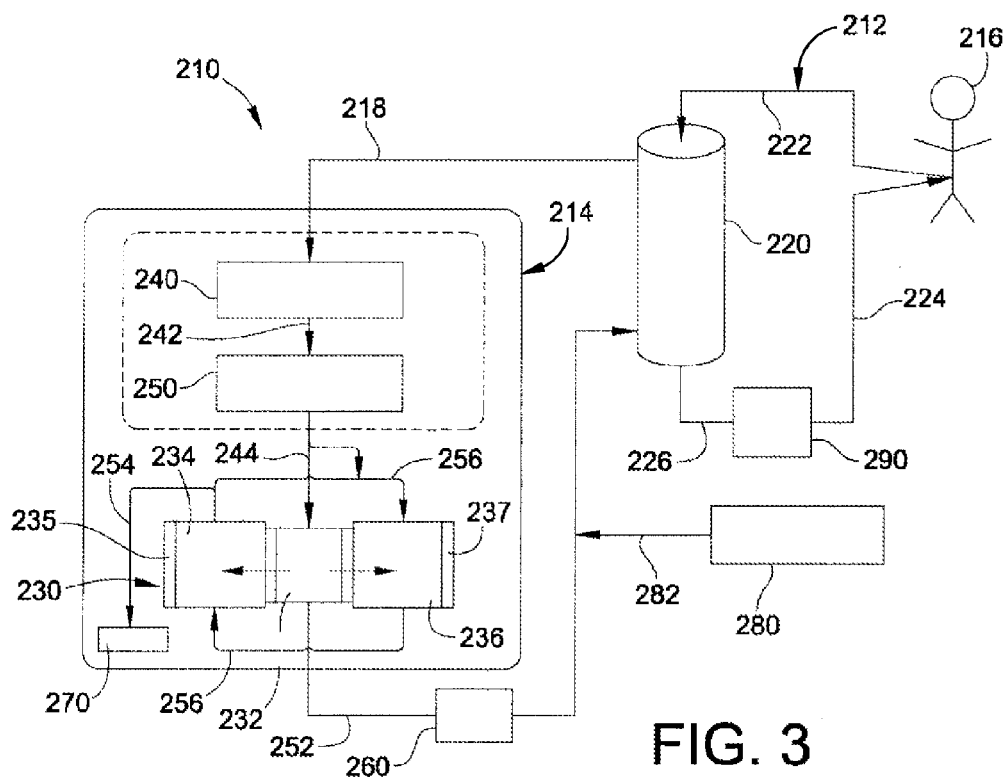


FIG. 2



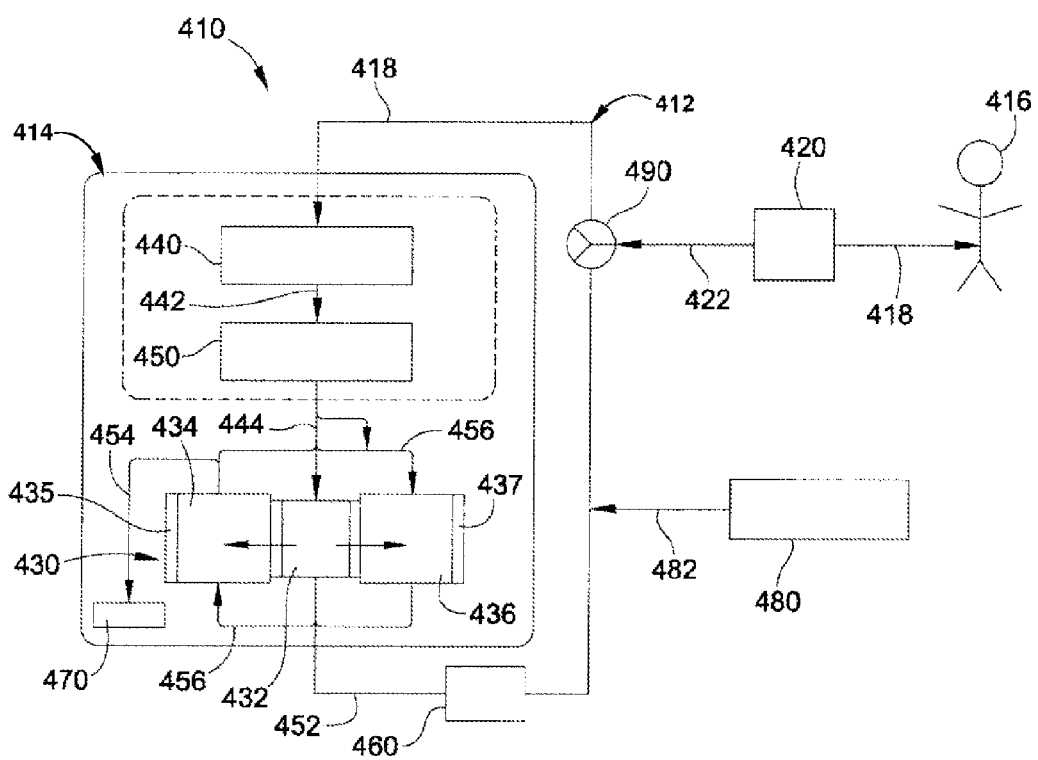


FIG. 5

FIG. 6

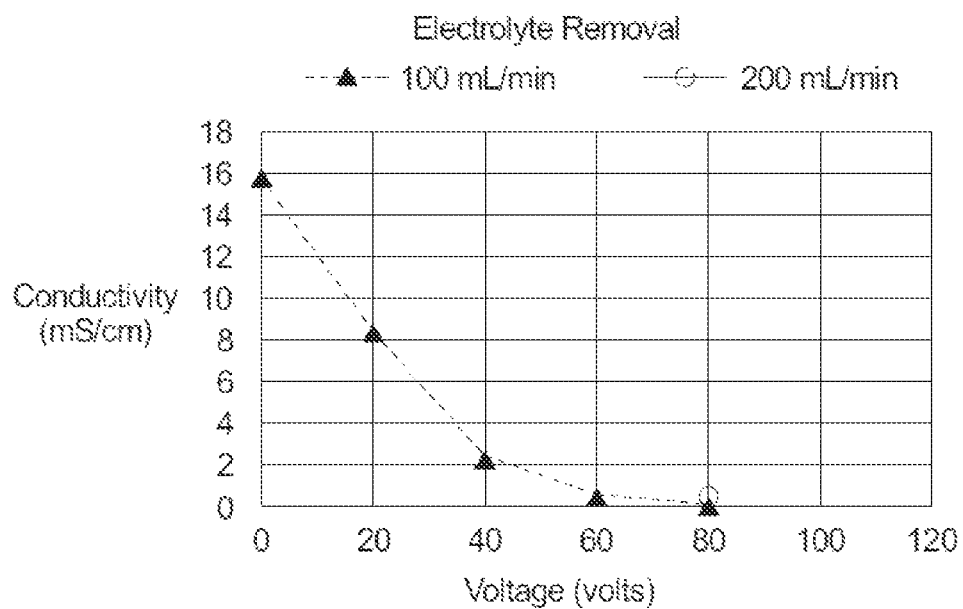


FIG. 7

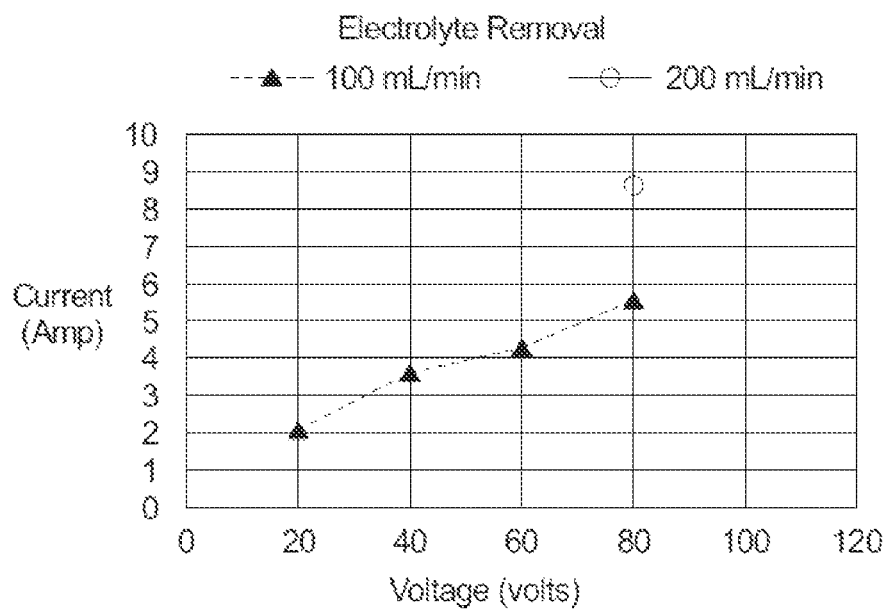


FIG. 8

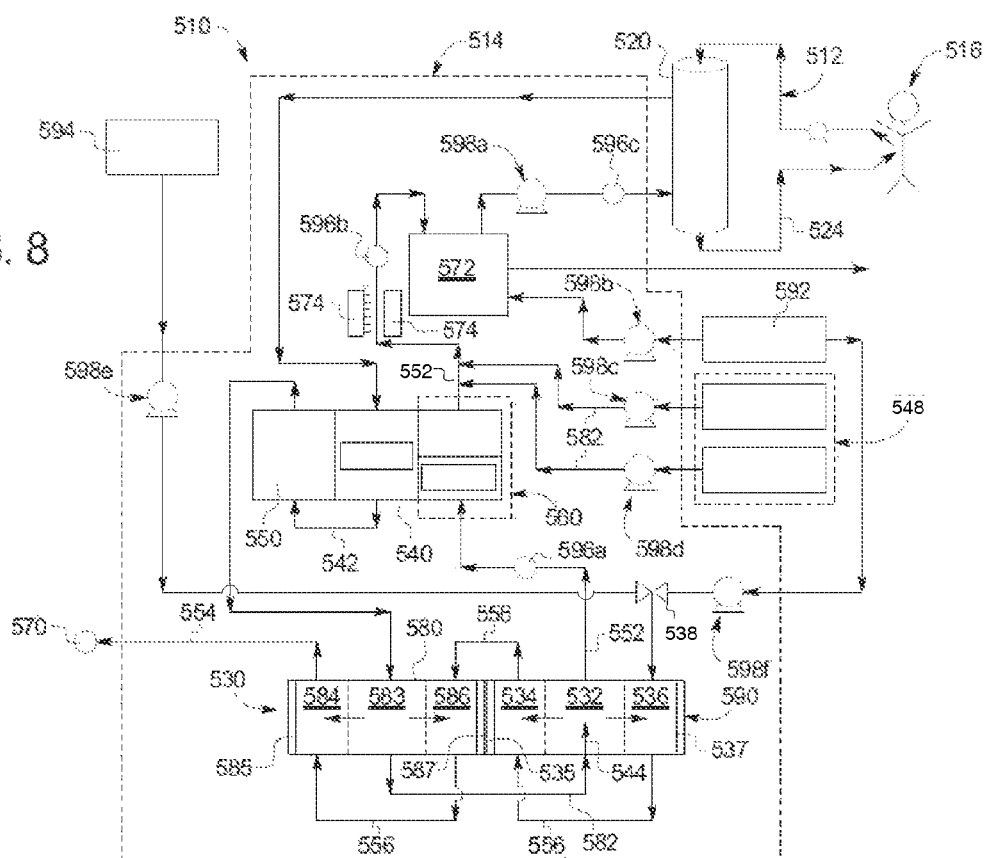


FIG. 9

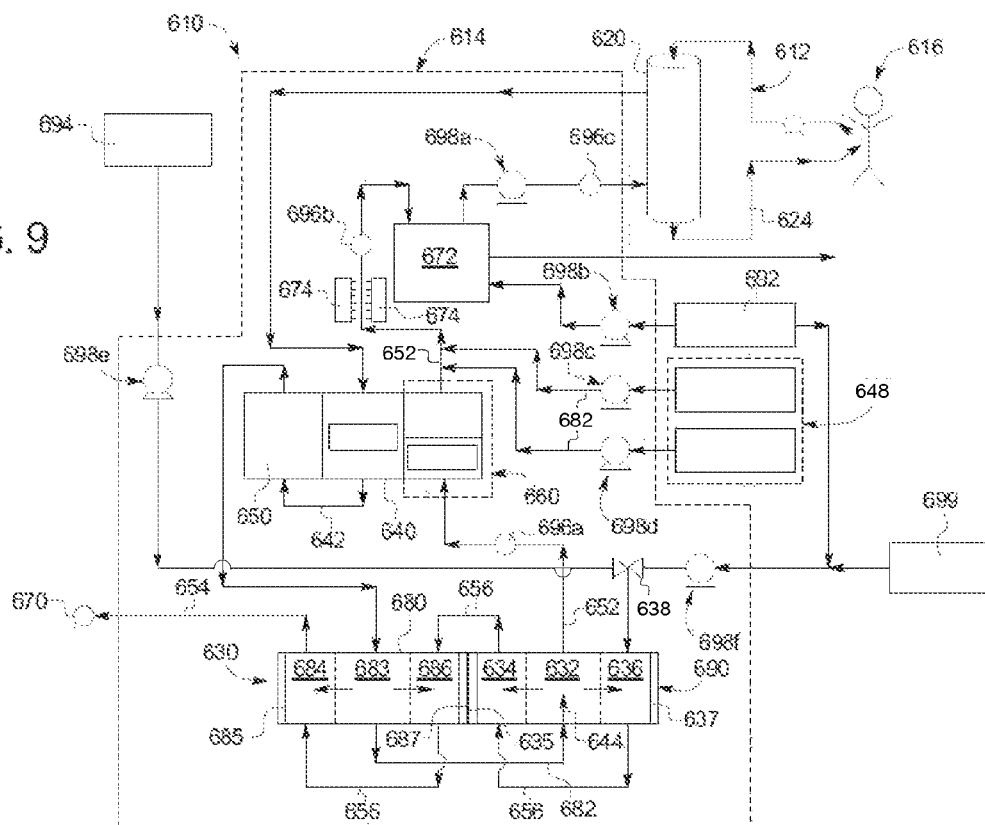


FIG. 10

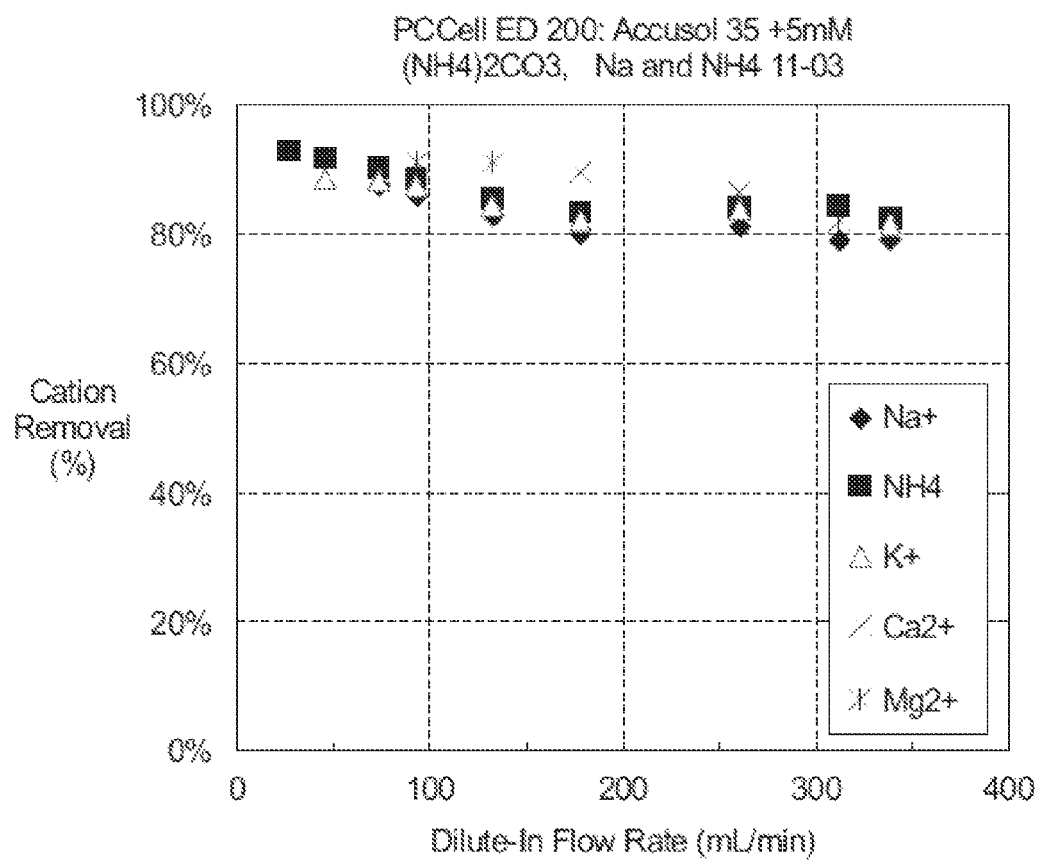


FIG. 11

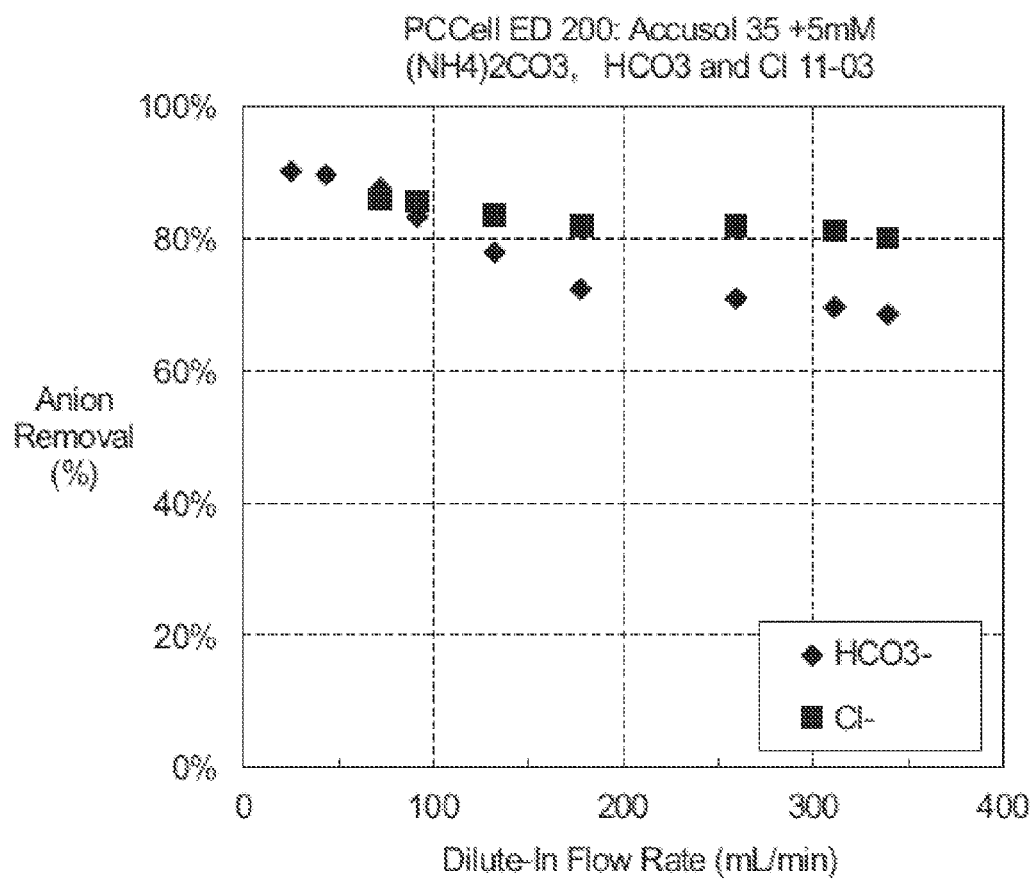


FIG. 12

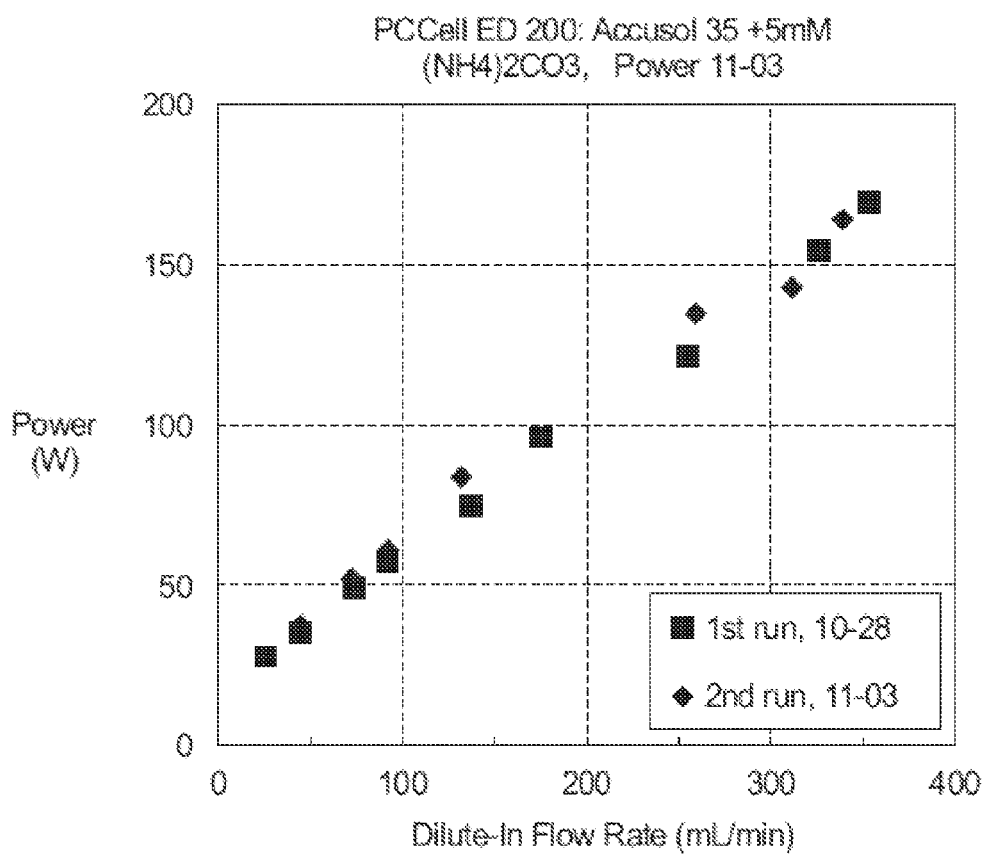


FIG. 13

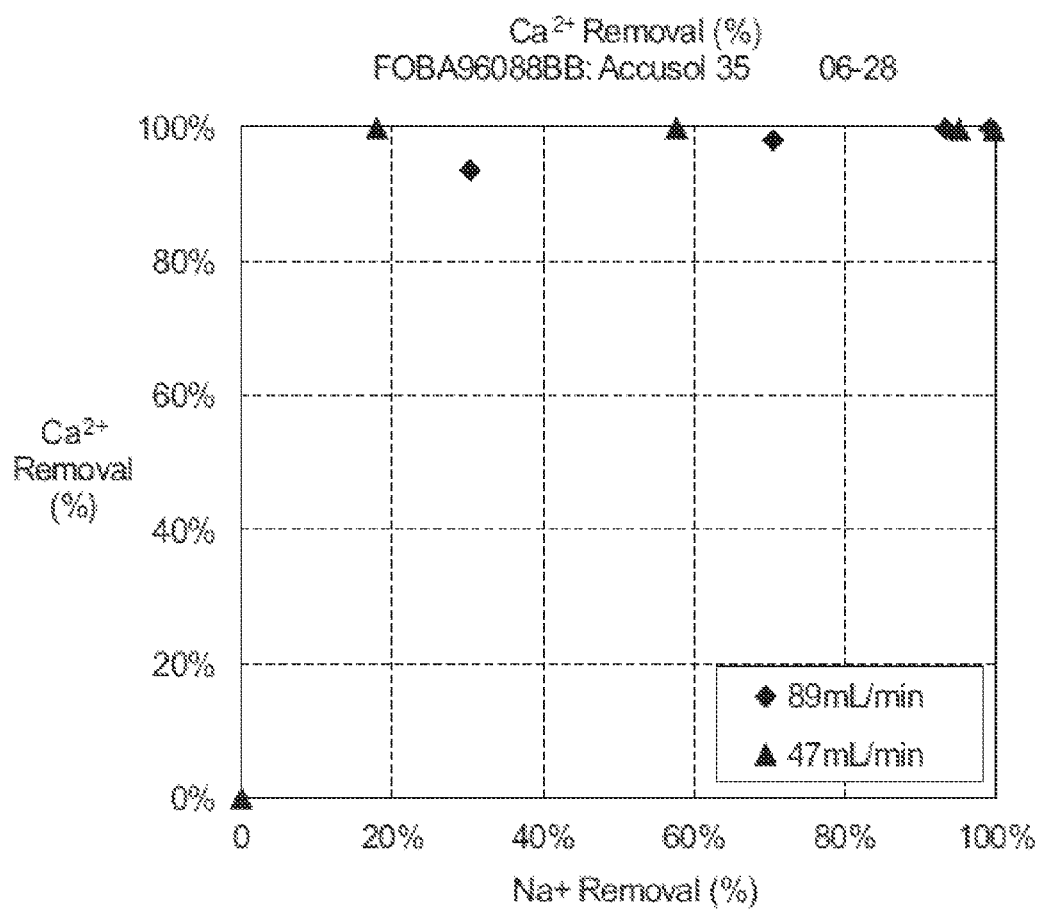


FIG. 14

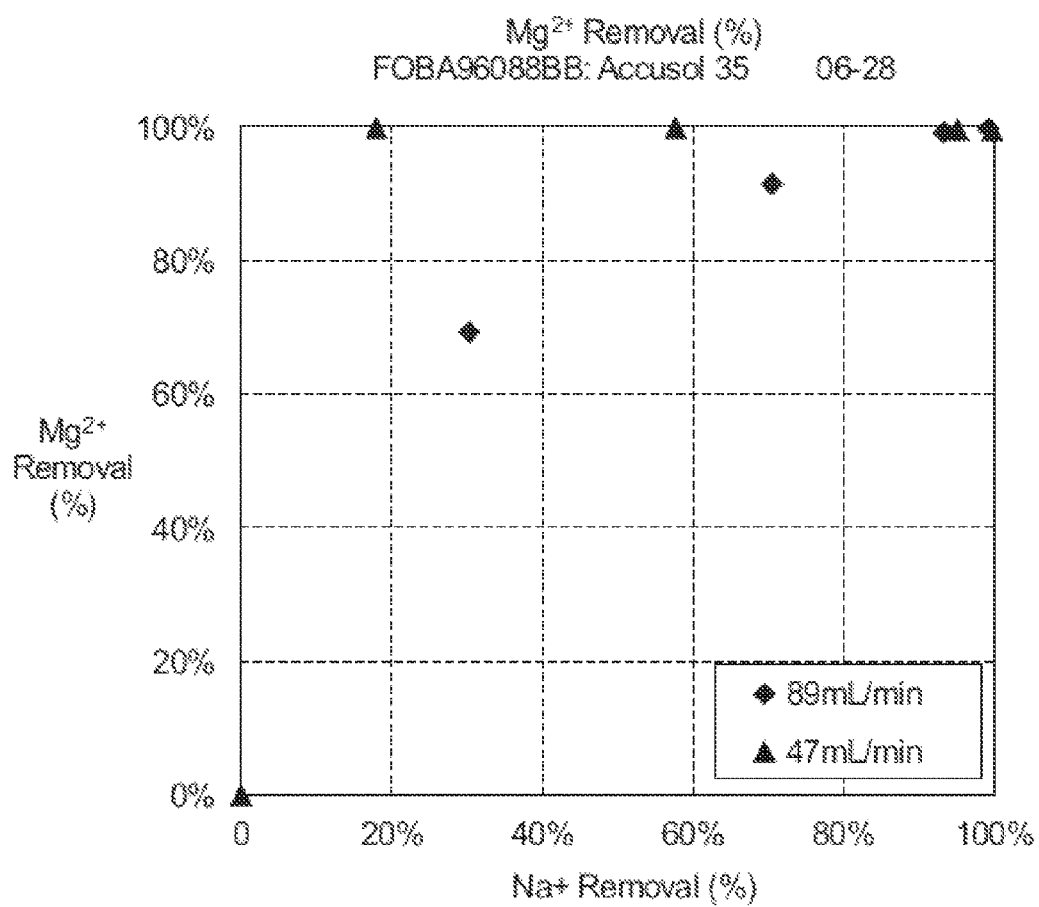


FIG. 15

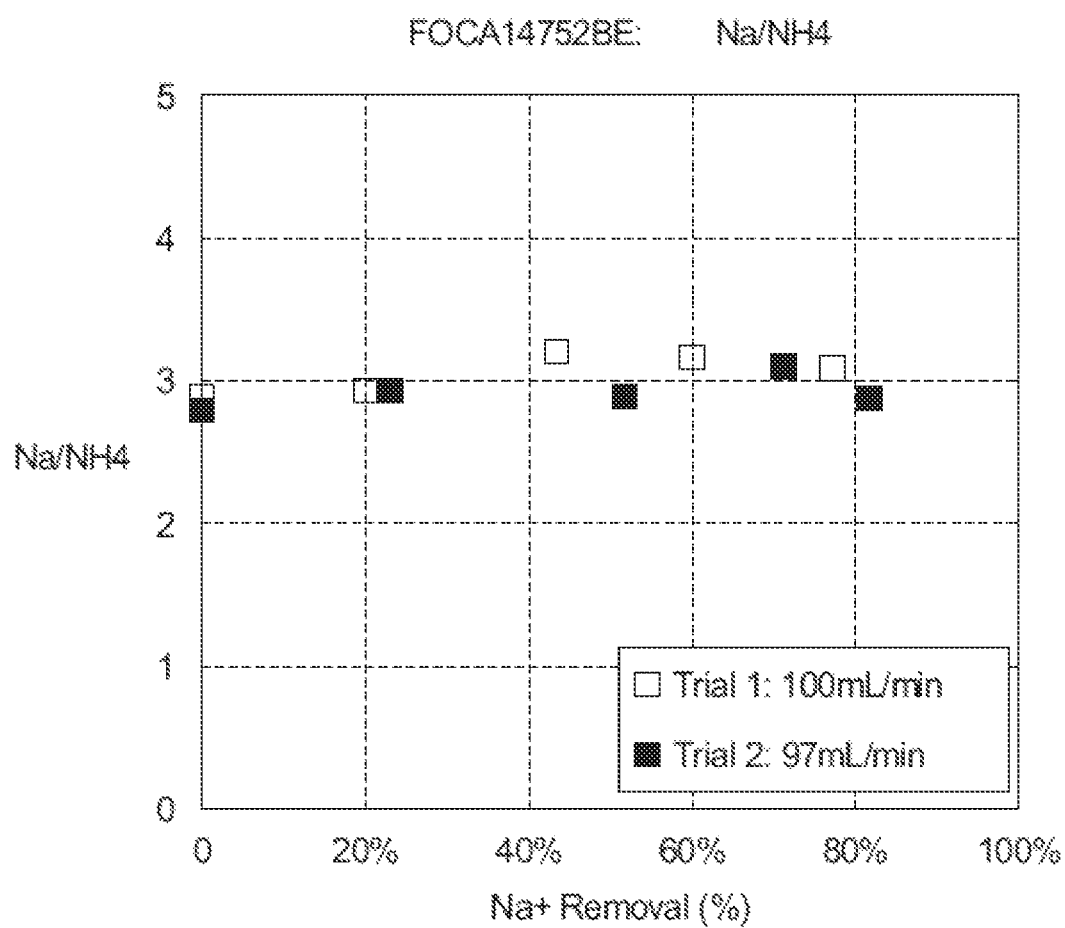


FIG. 16

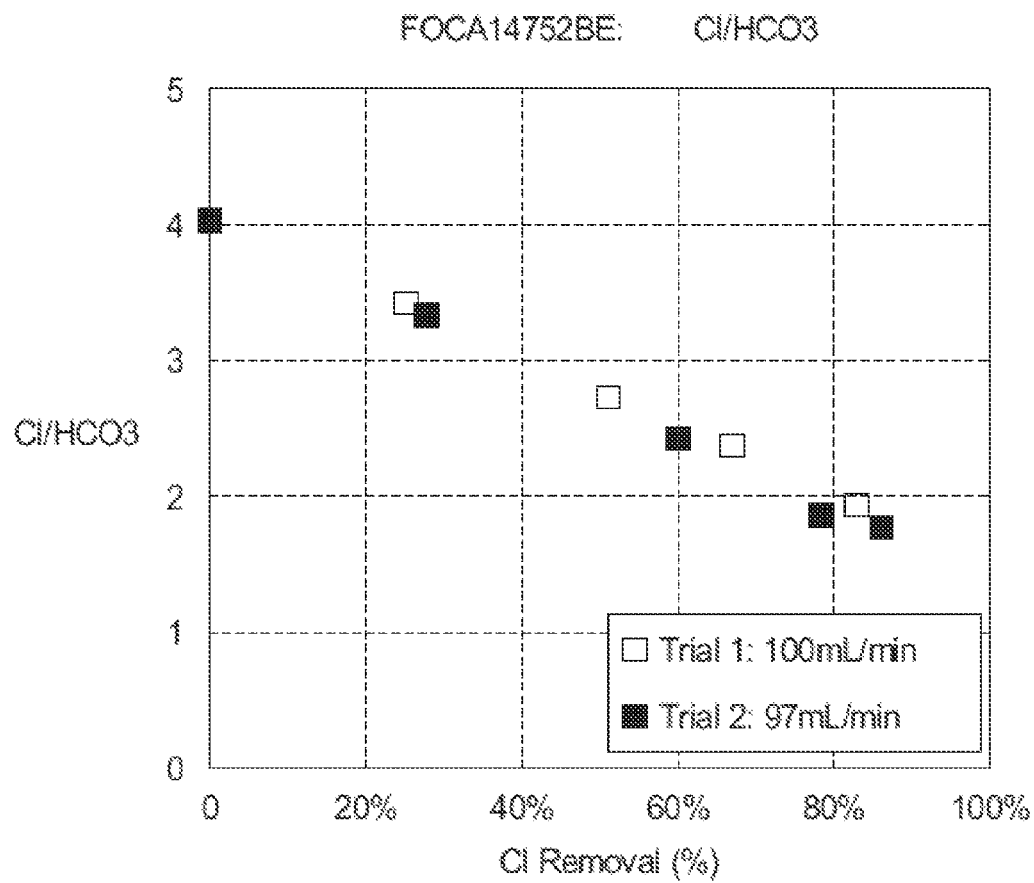


FIG. 17A

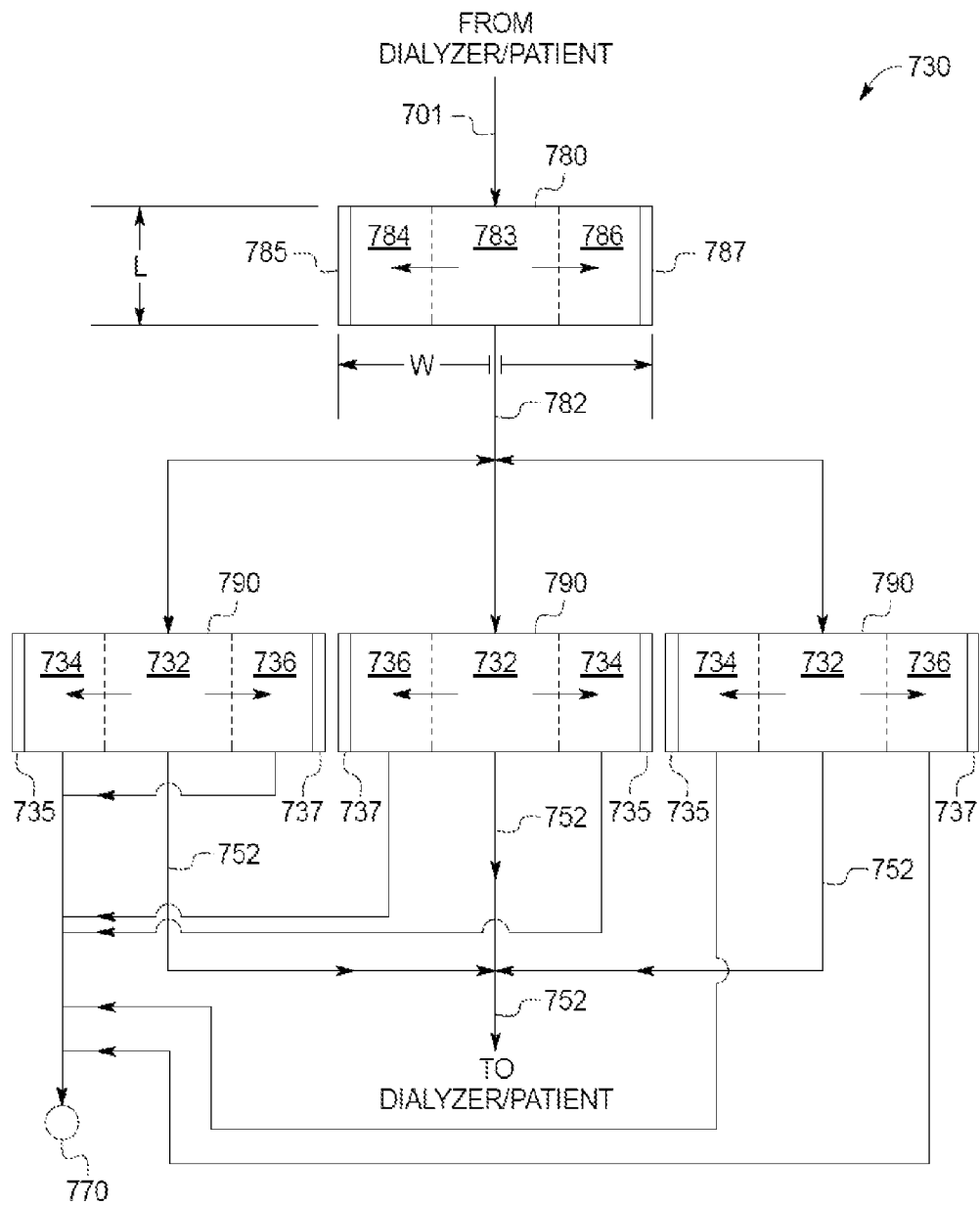
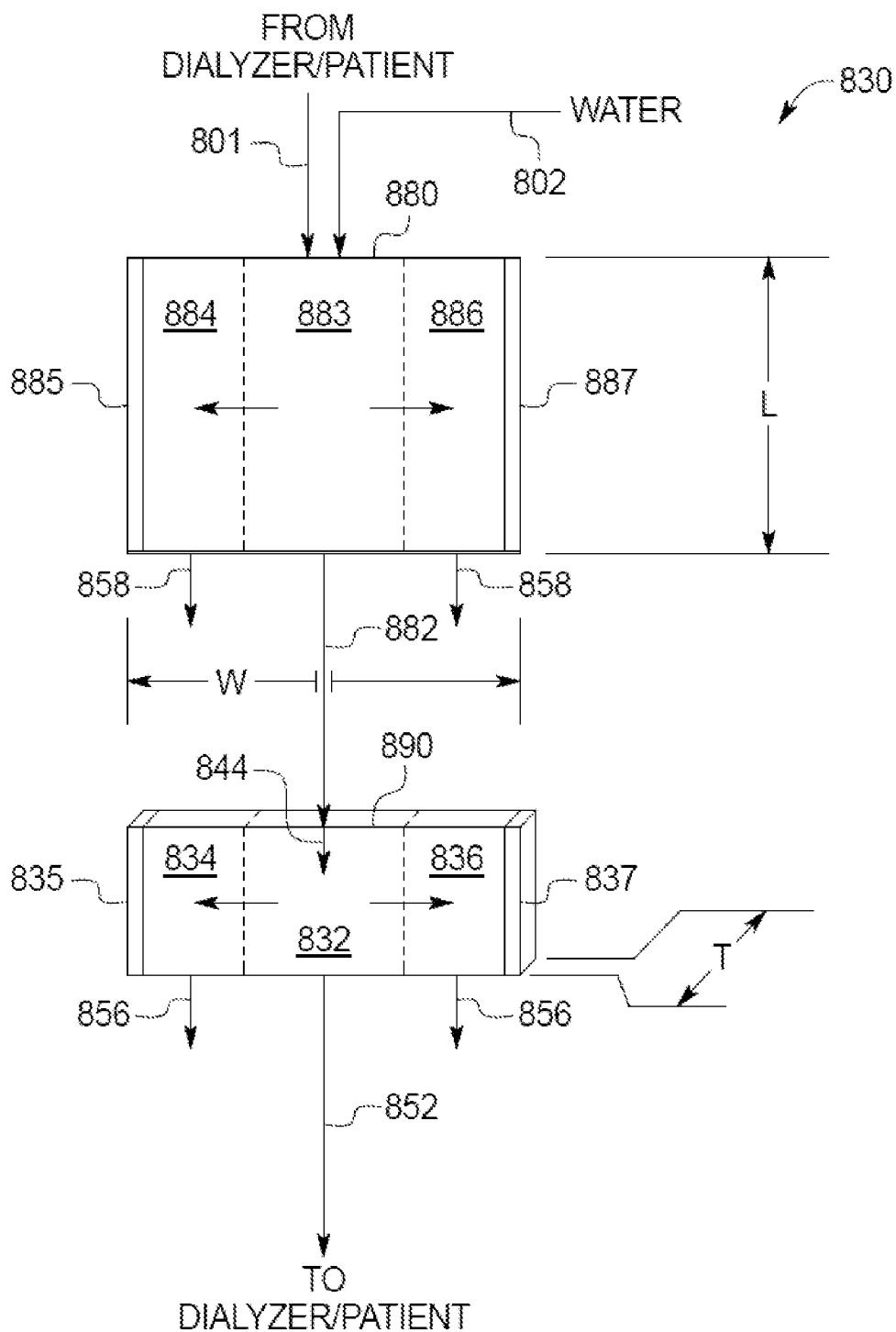


FIG. 17B



1

HEMODIALYSIS AND PERITONEAL DIALYSIS SYSTEMS HAVING ELECTRODIALYSIS AND ELECTRODEIONIZATION CAPABILITIES

PRIORITY CLAIM

This application claims priority to and the benefit as a continuation of Ser. No. 13/796,799, filed Mar. 12, 2013, now U.S. Pat. No. 9,005,440, which in turn claims priority to and the benefit as a continuation-in-part of U.S. patent application Ser. No. 12/718,609, filed Mar. 5, 2010, now U.S. Pat. No. 8,858,792, which in turn claims priority to U.S. Provisional Patent Application No. 61/158,101, filed Mar. 6, 2009, the entire contents of each of which are expressly incorporated herein by reference.

BACKGROUND

The present disclosure generally relates to dialysis systems. More specifically, the present disclosure relates to systems and methods for hemodialysis or peritoneal dialysis that recycle used dialysate through an electro dialysis- and electrodeionization-based regeneration system. These systems can perform high volume dialysis treatments without using large volumes of fresh dialysis fluid.

In both hemodialysis (“HD”) and peritoneal dialysis (“PD”), two general classes of dialysis systems currently exist. The first class uses fresh fluid (e.g., from a solution bag or some sort of water purification system) to generate dialysis fluid that is used to dialyze the individual. The second class uses “sorberent” technology to remove uremic toxins from waste dialysate. Therapeutic agents such as ions and/or glucose can be injected into the treated dialysate, which is used to continue the dialysis of the individual. The main advantage of the sorberent based approach is that very low volumes of fluid are required to achieve high volume dialysis treatments.

Disadvantages of sorberent systems include their high cost, disposability, and concerns regarding the purity of the recycled solution, as many ions remain in the fluid after treatment and verification of purity is technically challenging to perform. For example, sorberents can have high cartridge costs, insufficient removal of all of the tap water impurities, and insufficient removal of all of the uremic toxins in the used dialysate (e.g., sulfate). In addition, possible chemicals may be released or leached from the sorberent cartridge (e.g., zirconium). There may also be potential issues with pH and sodium balance.

SUMMARY

The present disclosure relates to systems and methods for hemodialysis, hemofiltration, hemodiafiltration or peritoneal dialysis having integrated electro dialysis (“ED”) and electrodeionization (“EDI”) capabilities. The ED/EDI systems and methods can further be utilized in portable dialysis devices such as wearable artificial kidneys. In a general embodiment, the dialysis system includes a carbon source, a urease source, and an ED/EDI unit. The carbon source, urease source, and/or the ED/EDI unit can be in the form of removable cartridges. The ED/EDI approach maintains the advantage of low fluid use in a sorberent system, but addresses the key shortcomings of the sorberent system. The ED/EDI technology is re-usable over very long periods of time (e.g., 5 to 7 years) thereby reducing cost, and essentially removes

2

all ionic contaminants from the waste dialysate (not just selective ions), resulting in verifiably pure recycled solution.

In another embodiment, the disclosure provides a method of performing hemodialysis. The method comprises passing a spent dialysis fluid from a dialyzer through a carbon source, a urease source and an ED/EDI unit to produce a clean dialysis fluid, and passing the clean dialysis fluid through the dialyzer. The clean dialysis fluid can pass through an ion exchange unit before passing through the dialyzer. In addition, one or more dialysis components can be added to the clean dialysis fluid before the clean dialysis fluid passes through the dialyzer.

In an alternative embodiment, the present disclosure provides a method of performing peritoneal dialysis. The method comprises passing a spent dialysis fluid from an individual through a carbon source, a urease source and an ED/EDI unit to produce a clean dialysis fluid, and returning the clean dialysis fluid to the individual. The clean dialysis fluid can pass through an ion exchange unit before returning to the patient. One or more dialysis components can be added to the clean dialysis fluid before returning to the individual. The clean dialysis fluid can also pass through a filter or an ultraviolet bactericidal light returning to the patient.

In yet another embodiment, the present disclosure provides a method of performing dialysis. The method comprises passing a spent dialysis fluid through a dialysis compartment of a dialyzer including an ion-rejection membrane that allows the passage of negatively charged ions and nonionic species but restricts the passage of positively charged ions. The ion-rejection membrane separates the dialysis compartment from a dialysate compartment of the dialyzer. The method further comprises passing used dialysis fluid generated from the dialysate compartment of the dialyzer through a carbon source, a urease source and an ED/EDI unit to produce a clean dialysis fluid. A source containing any desired negative ions is then added to the clean dialysis fluid. The clean dialysis fluid passes through the dialysate compartment of the dialyzer.

In an alternative embodiment, the ion-rejection membrane allows the passage of positively charged ions and nonionic species but restricts the passage of negatively charged ions. In this regard, a source containing any desired positive ions is then added to the clean dialysis fluid.

An advantage of the present disclosure is to provide an improved blood treatment, e.g., hemodialysis system.

Another advantage of the present disclosure is to provide an improved peritoneal dialysis system.

Yet another advantage of the present disclosure is to provide a dialysis system that has a high purity of recycled dialysis fluid.

Still another advantage of the present disclosure a dialysis system having low operating costs.

Additional features and advantages are described herein, and will be apparent from, the following Detailed Description and the figures.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 illustrates a schematic of a dialysis fluid recycling system for hemodialysis in an embodiment of the present disclosure.

FIG. 2 illustrates a schematic of a dialysis fluid recycling system for peritoneal dialysis in an embodiment of the present disclosure.

FIG. 3 illustrates a schematic of a dialysis fluid recycling system in another embodiment of the present disclosure.

3

FIG. 4 illustrates a schematic of a dialysis fluid recycling system for peritoneal dialysis in an embodiment of the present disclosure.

FIG. 5 illustrates a schematic of a dialysis fluid recycling system for peritoneal dialysis in another embodiment of the present disclosure.

FIG. 6 is a graph showing the conductivity of a dialysis solution treated using an EDI unit versus the operating voltage of the EDI unit.

FIG. 7 is a graph showing the operating current of an EDI unit versus the operating voltage of the EDI unit.

FIG. 8 is a schematic of a dialysis fluid recycling system in another embodiment of the present disclosure.

FIG. 9 is a schematic of a dialysis fluid recycling system in a further embodiment of the present disclosure.

FIG. 10 is a graph showing removal of sodium, ammonium, potassium, calcium and magnesium cations as a function of flow rate for a dialysis fluid treated using an ED/EDI combination unit in one embodiment of the present disclosure.

FIG. 11 is a graph showing removal of hypochlorite and chloride anions as a function of flow rate for a dialysis fluid treated using an ED component of an ED/EDI unit in one embodiment of the present disclosure.

FIG. 12 is a graph showing power consumption versus the flow rate for an ED component of an ED/EDI unit in one embodiment of the present disclosure.

FIG. 13 is a graph showing removal of calcium versus sodium cations at two flow rates using an EDI component of an ED/EDI unit according to one embodiment of the present disclosure.

FIG. 14 is a graph showing removal of magnesium versus sodium cations at two flow rates using an EDI component of an ED/EDI unit according to one embodiment of the present disclosure.

FIG. 15 is a graph showing the ratio of sodium to ammonium removed versus percentage of sodium cations removed at two flow rates using an EDI component of an ED/EDI unit according to one embodiment of the present disclosure.

FIG. 16 is a graph showing the ratio of chloride to hypochlorite removed versus percent of chloride anions removed at two flow rates using an EDI component of an ED/EDI unit according to one embodiment of the present disclosure.

FIG. 17A is a schematic illustration of one embodiment of a combination ED/EDI unit including commercially available ED unit and three commercially available EDI units.

FIG. 17B is a schematic of a combination ED/EDI unit according to another embodiment of the present disclosure.

DETAILED DESCRIPTION

The present disclosure relates to systems and methods for hemodialysis or peritoneal dialysis having integrated electrodialysis ("ED") and electrodeionization ("EDI") capabilities. In alternative embodiments, the ED/EDI systems and methods can be utilized and implemented in various hemodialysis and peritoneal dialysis technologies. Such dialysis systems are described in U.S. Pat. Nos. 5,244,568, 5,350, 357, 5,662,806, 6,592,542 and 7,318,892, which are incorporated herein by reference. The ED/EDI systems and methods can further be utilized in portable dialysis devices such as, for example, wearable artificial kidneys in which an individual may move freely during dialysis. Portable dialysis devices are described in U.S. Pat. Nos. 6,196,992, 5,873,853 and 5,984,891, which are incorporated herein by

4

reference. The ED/EDI systems and methods can be used in medical centers and be implemented with on-site or at-home dialysis treatments.

It should be appreciated that the EDI components of the ED/EDI units discussed herein differ from electrodialyzers (e.g., ED components). There are major differences between electrodialysis and EDI. An electrodialyzer is used to remove electrolytes from an aqueous feed solution introduced into a diluate chamber. An example of an electrolyte is NaCl. However, the level of electrolyte removal is not allowed to go below a certain limit. If one goes to a lower limit with very few electrolyte-based ions left in the solution, water splitting occur (also known as "electrolysis"), and a considerable amount of energy is wasted in splitting the water. This water splitting is needed for the current to flow between the electrodes maintained in the electrodialysis stack. The proton and the hydroxyl ion resulting from the water splitting will carry the current. It is to be avoided for a variety of reasons.

An electrodeionizer is an electrodialyzer in which the diluate channel into which the feed solution is introduced is filled with a bed of mixed ion exchange resin beads. At the top of the channel where the feed solution is introduced, the electrolytes present in the feed solution carry the current. Even though the ion exchange resin beads are there, they do not serve much of a deionization function. The mixed ion exchange resin beads in the electrodeionizer enhance the efficiency of removing the electrolytes from the dialysate solution as well as alleviate the effects of water splitting as a result of little to no electrolytes remaining in the solution further down the channel.

For each of the embodiments discussed herein, the ED and EDI units, whether integrated or separate, can be made of metal, plastic, or some combination thereof. If plastic, the plastic is a medical grade plastic, such as polyvinyl chloride ("PVC"). If metal, the ED and EDI units can be stainless steel. Regardless of material, the ED and EDI units can be reused or be single use. For example, a metal version of the ED and EDI units can be hot water or steam disinfected after a treatment and be reused, say for another hemodialysis or blood treatment. Plastic and hybrid metal/plastic units can also be disinfected for reuse. In another example, a plastic version of the ED and EDI units can be used a single time, e.g., for peritoneal dialysis, and then discarded.

Systems of the Present Disclosure

In a general embodiment, a dialysis fluid recycling system 10 for hemodialysis is illustrated in FIG. 1. As shown in FIG. 1, a circuit 12 represents a standard blood circuit for a hemodialysis machine. Circuit 12 cycles blood from an individual 16 via flow path 22 through a dialyzer 20 and returns it to the individual's body via flow path 24. Dialyzer 20 can include a dialysate compartment and a blood compartment separated by a suitable membrane. A circuit 14 includes an EDI unit or module 30 in dialysis fluid recycling system 10. Module 30 can be constructed and used once or reused as described above. Circuit 14 can also include a carbon source 40 and a urease source 50 connected to carbon source 40 via flow path 42. Carbon source 40, urease source 50, and/or EDI unit 30 can be in the form of one or more removable cartridge, such as part of a disposable or reusable pumping and/or valving cartridge.

EDI unit 30 can include a central chamber 32, an anion chamber 34 having an anode 35, and a cation chamber 36 having a cathode 37. As fluid exiting urease source 50 flows to central chamber 32 via flow path 44, a potential difference

5

between anode **35** and cathode **37** causes the electrolytes in the fluid in central chamber **32** to flow into anion chamber **34** and cation chamber **36**. Specifically, negatively charged ions flow into anion chamber **34** while positively charged ions flow into cation chamber **36** where they are subsequently removed. The treated fluid that passes through EDI unit **30** exits as part of a treated fluid stream via flow path **52**. A waste fluid stream filled with electrolytes exits via flow path **54** that can lead to a drain **70**.

EDI unit **30** can also be modified so that a suitable quantity of fluid can be recirculated around EDI unit **30** via flow path **56**. This reduces the amount of fluid flowing through EDI unit **30** that would end up as part of the waste fluid stream. As a result, a higher quantity of fluid exits as the treated fluid stream as compared to the quantity of treated fluid from an EDI unit without recirculation.

During operation, after priming system **10** with an appropriate amount of fluid (in this case, priming fluid can be any of, dialysis fluid, sterile bagged water, tap water in its raw form, tap water purified through standard means such as deionization and/or reverse osmosis, or a combination therein), the dialysis solution is recirculated through circuit **14** via flow path **18** in the direction indicated. Used dialysis fluid leaves dialyzer **20** saturated with uremic toxins, as well as normal dialysis fluid components such as dextrose and ions (e.g., sodium, calcium, magnesium, etc.). The organic toxins of the fluid, as well as the lactate or bicarbonate buffer of the solution, are then removed from the fluid through adsorption onto a carbon surface (e.g. activated carbon or other appropriate organic neutralizing surface) of carbon source **40**.

Urea, which is not well removed by carbon, is then exposed to urease source **50**. Urease is an enzymatic catalyst which facilitates the breakdown of urea into ammonium and ammonia (e.g., depending on pH). Urease source **50** can be immobilized on any suitable surface that allows the passage of a liquid or be a membrane impregnated with cross-linked urease enzyme crystals.

The pKa of ammonium ion is 9.25. For efficient removal, the pH needs to be below neutral. At lower pH's, a greater portion of ammonia will be in ionized form. Passing it through an optional cation exchanger will help lower the pH and have better removal of ammonia. Removal of the ammonium in can also be accomplished within EDI unit **20**.

After the fluid has passed through urease source **50**, all organic contaminants will have been adsorbed or broken down into ionic contaminants before entering EDI unit **30**. In EDI unit **30**, ions are removed from the fluid through electromagnetic facilitated transport through cation and anion selective membranes. The fluid that exits EDI unit **30**, in contrast to currently existing sorbent systems, contains very few ions, e.g., with nominal fluid resistivity approaching or in excess of 5 MΩ·cm. In this regard, EDI unit **30** can render the zirconium phosphate layer, zirconium bicarbonate layer and/or ion exchange layer typically used for ammonium/ion removal unnecessary.

After EDI unit **30**, ions and/or fluids can be replaced in the clean fluid stream through the addition of one or more concentrated dialysis components from a concentrate or fluid metering source **80** via flow path **82**. The concentrated dialysis components can include one or more osmotic agents (e.g., dextrose, icodextrin, glucose polymers, glucose polymer derivatives, amino acids), buffers (e.g., lactate, bicarbonate) and electrolytes (e.g. sodium, potassium, calcium, magnesium) from a small fluid source. After this addition, the fluid is compositionally equivalent to fresh dialysis

6

solution and can be used to remove additional uremic toxins from the individual's blood stream.

To further realize the benefits of EDI over existing sorbent systems, EDI unit **30** would not be expected to be replaced over the foreseeable lifetime of the hemodialysis systems/devices. Carbon source **40** and urease source **50** can be replaced at some determined interval, but these are much lower cost components than sorbent cartridges and do not negatively impact the economic benefits of the system. Alternatively, EDI unit **30** can be provided in the form of a removable or disposable cartridge, such as part of a disposable or reusable pumping and/or valving cassette.

In an embodiment shown in FIG. 1, additions can be made to enhance the functionality and/or safety of the system. For example, biological purity of system **10** can be assured through replacement of circuits **12** and **14** after each treatment, along with dialyzer **20**. However, circuits **12** and **14** can also be re-used for multiple treatments if suitable disinfection and sanitization methods were undertaken. These can include all currently accepted methods, such as heat sanitization, chemical sanitization (including ozonation), addition of ultraviolet ("UV") bactericidal lights, and the addition of additional dialyzers and/or ultrafilters in the system with a pore size appropriate for the removal of bacterial and sub-bacterial contaminants.

The monitoring of system **10** can be enhanced through the inclusion of an optional ammonia sensor in the loop after EDI unit **30** to ensure that all ammonia has been removed. Because fluid of resistance approaching 5 MΩ·cm can be made after passing through EDI unit **30**, an optional conductivity sensor may be used to assure there is no ammonia versus the traditional approach of using an ammonia sensor. Finally, one or more optional ion exchanger unit **60** that have low cost and/or high capacity can be used to supplement EDI unit **30** to improve its performance or reduce its necessary size. These optional ion exchangers can include a phosphate removal exchanger with a bicarbonate counter ion to enhance phosphate removal or a cation exchanger that helps to remove any remaining ammonia.

The dialyzers in any embodiments of the present disclosure can include an ion-rejection membrane that allows the passage of negatively charged ions and nonionic species but restricts the passage of positively charged ions. Alternatively, the dialyzers in any embodiments of the present disclosure can include an ion-rejection membrane that allows the passage of positively charged ions and nonionic species but restricts the passage of negatively charged ions.

In another embodiment, a dialysis fluid recycling system **110** for peritoneal dialysis is illustrated in FIG. 2. As shown in FIG. 2, a circuit **112** cycles spent dialysis fluid from an individual **116** via flow path **122** through a dialyzer **120** and returns it to the individual's body via flow path **124**. Dialyzer **120** can include a dialysate compartment and a peritoneal dialysis fluid compartment separated by a suitable membrane. A circuit **114** includes an EDI unit **130** in the dialysis fluid recycling system. EDI unit **130** can be constructed to be reused or used once as described above. Fluid from dialyzer **120** transfers to circuit **114** via flow path **118**.

Circuit **114** can also include a carbon source **140** and a urease source **150** connected to carbon source **140** via flow path **142**. Circuit **114** can further include an optional ion exchange unit **160** in fluid connection with EDI unit **130** via flow path **152**. Flow path **152** can lead directly back to dialyzer **120**. Carbon source **140**, urease source **150**, ion exchange unit **160**, and/or EDI unit **130** can be in the form of one or more removable cartridge, such as part of a disposable or reusable pumping and/or valving cassette.

EDI unit **130** can include a central chamber **132**, an anion chamber **134** having an anode **135**, and a cation chamber **136** having a cathode **137**. As fluid flows through central chamber **132** via flow path **144**, a potential difference between anode **135** and cathode **137** causes the electrolytes in the fluid in central chamber to flow into anion chamber **134** and cation chamber **136**. The treated fluid that passes through EDI unit **130** exits as part of a treated fluid stream **152** that leads back to dialyzer **120**. A waste fluid stream filled with electrolytes exits via flow path **54** that leads to a drain **170**.

EDI unit **130** can also be modified so that a suitable quantity of fluid can be recirculated around EDI unit **130** via flow path **156**. This reduces the amount of fluid flowing through EDI unit **130** that would end up as part of the waste fluid stream.

System **110** is nearly identical to the hemodialysis system **10** of FIG. **1**. However, in this embodiment, the solution being passed through circuit **112** represents peritoneal dialysis fluid, rather than individual's **116** own blood. The peritoneal dialysis procedure can be run, for example, in a "continuous flow" mode, where used dialysis fluid exits the individual's peritoneum as new fluid enters it through a dual lumen catheter. The used fluid is passed through dialyzer **120** where uremic toxins are removed and the waste fluid is treated just as it would be in hemodialysis. The composition of a concentrate addition to the fluid stream in flow path **152** from a concentrate or fluid metering source **180** via flow path **182** may be specifically tailored for peritoneal dialysis.

Additions to this type of system, along with those described for the hemodialysis system, can be included to enhance effectiveness or safety of the system. In an embodiment, the typical dialyzer membrane can be replaced with an ion-rejection membrane that allows the passage of negatively charged ions and nonionic species, but restricts the passage of positively charged ions (or vice versa). In this case, the peritoneal dialysis loop that is recirculating to the individual would be cleared of uremic toxins (which are neutrally or negatively charged), but the concentrate addition would not need to include replacement of the positive ions of the dialysis solution, which enhances the efficiency of the system.

In an alternative embodiment, a dialysis fluid recycling system **210** for hemodialysis or peritoneal dialysis is illustrated in FIG. **3**. As shown in FIG. **3**, a circuit **212** cycles fluid from an individual **216** through a dialyzer **220** and returns it to the individual's body. A circuit **214** includes an EDI unit or module **230** in the dialysis fluid recycling system. EDI unit or module **230** can be constructed to be used once or reused as described above.

Circuit **214** can also include a carbon source **240** and a urease source **250** connected to carbon source **240** via flow path **242**. Circuit **214** can further include an optional ion exchange unit **260** in fluid connection with EDI unit **230** via flow path **252**. Flow path **252** can lead directly back to dialyzer **220**. Carbon source **240**, urease source **250**, ion exchange unit **260**, and/or EDI unit **230** can be in the form of one or more removable cartridge, such as part of a disposable or reusable pumping and/or valving cassette.

EDI unit **230** can include a central chamber **232**, an anion chamber **234** having an anode **235**, and a cation chamber **236** having a cathode **237**. As fluid flows through central chamber **232** via flow path **244**, a potential difference between anode **235** and cathode **237** causes the electrolytes in the fluid in central chamber to flow into anion chamber **234** and cation chamber **236**. The treated fluid that passes through EDI unit **230** exits as part of a treated fluid stream

252. A waste fluid stream filled with electrolytes exits via flow path **254** that leads to a drain **270**.

EDI unit **230** can also be modified so that a suitable quantity of fluid can be recirculated around EDI unit **230** via flow path **256**. This reduces the amount of fluid flowing through EDI unit **230** that would end up as part of the waste fluid stream.

After leaving EDI unit **230** via flow path **252**, one or more dialysis components from a concentrate or fluid metering source **280** via flow path **282** may be specifically tailored for the specific type of dialysis performed. An additional purification or treatment component **290** in the form of a filter or ultraviolet bactericidal light can be added to circuit **212**, as shown in FIG. **3**. Fluid exiting dialyzer **220** via flow path **226** can be further filtered or subject to a bactericidal light to enhance the bacterial purity of system **210**. The treated fluid can then enter individual **216** via flow path **224**. Purification component **290** can be especially important to peritoneal dialysis because bacterial contamination is a significant concern for the treatment.

In yet another embodiment, a dialysis fluid recycling system **310** for peritoneal dialysis is illustrated in FIG. **4**. As shown in FIG. **4**, a circuit **312** cycles blood from an individual **316** through a circuit **314**. In order to perform the peritoneal dialysis treatment as shown in FIG. **4**, flow path **318** of recycling system **310** can be constructed such that spent dialysis fluid from individual **316** is sent directly to recycling system **310** without the need for "dialyzing" the PD fluid. The peritoneal dialysis procedure can be run, for example, in a "continuous flow" mode.

Circuit **314** includes an EDI unit or module **330** in the dialysis fluid recycling system. EDI unit or module **330** can be constructed to be used once or reused as described above. Circuit **314** can also include a carbon source **340** and a urease source **350** connected to carbon source **340** via flow path **342**. Circuit **314** can further include an optional ion exchange unit **360** in fluid connection with EDI unit **330** via flow path **352**. Flow path **352** can lead directly back to dialyzer **320**. Carbon source **340**, urease source **350**, ion exchange unit **360**, and/or EDI unit **330** can be in the form of one or more removable cartridge, such as part of a disposable or reusable pumping and/or valving cartridge.

EDI unit **330** can include a central chamber **332**, an anion chamber **334** having an anode **335**, and a cation chamber **336** having a cathode **337**. As fluid flows through central chamber **332** via flow path **344**, a potential difference between anode **335** and cathode **337** causes the electrolytes in the fluid in central chamber to flow into anion chamber **334** and cation chamber **336**. The treated fluid that passes through EDI unit **330** exits as part of a treated fluid stream **352**. A waste fluid stream filled with electrolytes exits via flow path **354** that leads to a drain **370**.

EDI unit **330** can also be modified so that a suitable quantity of fluid can be recirculated around EDI unit **330** via flow path **356**. This reduces the amount of fluid flowing through EDI unit **330** that would end up as part of the waste fluid stream.

After leaving EDI unit **330** via flow path **352**, one or more dialysis components from a concentrate or fluid metering source **380** via flow path **382** may be specifically tailored for the type of dialysis performed. An additional purifying component **390** such as a filter, UV light, and/or other commonly accepted methods can optionally be used on the inlet line to the individual's **316** peritoneal cavity to prevent bacterial contamination and also on the line from the individual back to system **310** (not shown) to prevent retro-

contamination to individual **316**. The purified dialysis solution can be provided to individual **316** via flow path **322**.

In yet another embodiment, a dialysis fluid recycling system **410** for peritoneal dialysis is illustrated in FIG. 5. As shown in FIG. 5, a circuit **412** cycles dialysis fluid from an individual **416** to via flow path **422** to a three way valve **490**. From three-way valve **490**, the fluid flows to a circuit **414** via flow path **418** where the fluid is recycled. System **410** is designed to operate in a standard peritoneal dialysis therapy mode where fluid is injected, allowed to dwell, then removed from individual **416**. Once the dialysis fluid has been purified, the dialysis fluid is then sent back to individual **416** via flow path **418**, allowed to dwell, removed, purified, and repeated. The control of the flow direction can be accomplished with three-way valve **490** as shown in FIG. 5.

Circuit **414** includes an EDI unit **430**. EDI unit or module **430** can be constructed to be used once or reused as described above. Circuit **414** can also include a carbon source **440** and a urease source **450** connected to carbon source **440** via flow path **442**. Circuit **414** can further include an optional ion exchange unit **460** in fluid connection with EDI unit **430** via flow path **452**. Flow path **552** can lead directly back to dialyzer **420**. Carbon source **440**, urease source **450** and/or ion exchange unit **460** can be in the form of removable cartridges. After leaving EDI unit **430** via flow path **452**, one or more dialysis components from a concentrate or fluid metering source **480** via flow path **482** may be specifically tailored for the type of dialysis performed.

EDI unit **430** can include a central chamber **432**, an anion chamber **434** having an anode **435**, and a cation chamber **436** having a cathode **437**. As fluid flows through central chamber **432** via flow path **444**, a potential difference between anode **435** and cathode **437** causes the electrolytes in the fluid in central chamber to flow into anion chamber **434** and cation chamber **436**. The treated fluid that passes through EDI unit **430** exits as part of a treated fluid stream **452**. A waste fluid stream filled with electrolytes exits via flow path **454** that leads to a drain **470**.

EDI unit **430** can also be modified so that a suitable quantity of fluid can be recirculated around EDI unit **430** via flow path **456**. This reduces the amount of fluid flowing through EDI unit **430** that would end up as part of the waste fluid stream.

In still another alternative embodiment, a dialysis fluid system **510** for hemodialysis (or other blood treatment) or peritoneal dialysis, having recycling capabilities, is illustrated in FIG. 8. In this embodiment, the water source for regeneration of dialysate is an ultrapure, sterile or injectable quality water source **592**, which is fed via pump **598f** and associated valves to ED/EDI unit **530**. Water source can for example be a water purification machine, such as one set forth in U.S. Patent Publication No. 2011/0197971, entitled, "Water Purification System And Method", filed Apr. 25, 2011, the entire contents of which is incorporated herein by reference and relied upon. In some embodiments, about twelve to eighteen liters of ultrapure or sterile water per dialysis session are provided by sterile water source **592**. This twelve to eighteen liters of water is used to replenish fluid pumped or delivered to drain **570**.

As shown in FIG. 8, a blood or peritoneal dialysis fluid circuit **512** cycles fluid, e.g., from an individual **516** through a dialyzer **520** and returns the fluid to the individual's body. A dialysis fluid recirculation circuit **514** includes a combination ED/EDI unit or module **530**. A peritoneal dialysis application may use dialyzer **520** and separate circuits **512** and **514**. Here circuit **512** is sterile, while circuit **514** can be

less than sterile due to the separation by the membranes of dialyzer **520**. Alternatively, dialyzer **520** is removed and circuits **512** and **514** are merged into one another, eliminating structure and possibly a pump. Here, however, the fluid returning directly to the patient via the recirculation and cleaning loop needs to be sterile or injectable quality. The combination ED/EDI unit **530** includes an ED component **580** in fluid connection with an EDI component **590** via flow path **582**. ED/EDI unit or module **530** can be constructed to be used once or reused as described above.

The ED component **580** in the illustrated embodiment includes a central chamber **583**, an anion chamber **584** having an anode **585**, and a cation chamber **586** having a cathode **587**. As spent fluid flows through central chamber **583** via flow path **584**, a potential difference between anode **585** and cathode **587** causes the electrolytes in the fluid in central chamber **583** to flow or migrate into anion chamber **584** and cation chamber **586**. The treated fluid that passes through the ED component **580** enters the EDI component **590** via flow path **582**. A waste fluid stream filled with electrolytes exits ED component **580** via flow path **554** that leads to a drain **570**.

The EDI component **590** in the illustrated embodiment includes a central chamber **532**, an anion chamber **534** having an anode **535**, and a cation chamber **536** having a cathode **537**. EDI component **590**, and in the illustrated embodiment cation chamber **536** of component **590**, is in fluid connection at junction **538** with an acid solution or acid concentrate **594** and sterile water source **592**. System **510** includes valves (not illustrated), such as valves operating in conjunction with fluid pumps **598e** and **598f**, to selectively deliver acid concentrate and/or ultrapure, sterile or injectable water to EDI component **590**. As spent dialysate flows through central chamber **532** via flow path **544**, a potential difference between anode **535** and cathode **537** causes the electrolytes in the fluid in central chamber **532** to flow or migrate into anion chamber **534** and cation chamber **536**. The treated dialysis fluid that passes through the EDI component **590** exits as part of a treated fluid stream **552**.

The ED/EDI unit **530** can also be modified as illustrated so that a suitable quantity of fluid can be recirculated around the ED/EDI unit **530** via flow path **556**. In the illustrated embodiment, a separate bypass or recirculation path **536** is provided for both ED component **580** and EDI components **590**. Alternatively, a single bypass or recirculation line is provided for the entire ED/EDI unit **530**, which extends from anywhere within ED component **580** to anywhere within EDI component **590**. Recirculation reduces the amount of fluid flowing through ED/EDI unit **530** that would end up as part of the waste fluid stream discarded to drain **570**.

Dialysis fluid circuit **514** can also include a carbon source **540** and a urease source **550** connected to carbon source **540** via flow path **542**. Carbon source **540**, urease source **550**, ion exchange unit **560** (discussed below), and/or ED/EDI unit **530** can be provided in the form of one or more removable cartridges or cassettes, which may or may not also include ED/EDI unit **530**. In the illustrated embodiment, fluid exiting dialyzer **520** or the patient is fed first through carbon source **540** and urease source **550** before reaching ED/EDI unit **530**. Carbon source **540** and urease source **550** could be located alternately downstream of ED/EDI unit **530**.

Recirculation circuit **514** can further include an optional ion exchange unit **560** in fluid connection with ED/EDI unit **530** via flow path **552**. Flow path **552** leaving ion exchange unit **560** can lead directly back to dialyzer **520** or to a dialysate reservoir **572**, e.g., a bag or rigid container. Pump

11

598b and its associated valves pump and direct ultrapure, sterile or injectable quality water from source **592** into reservoir **572**. Pump **598a** and its associated valves pump and direct the cleaned and replenished dialysis fluid (e.g., from reservoir **572**) to dialyzer **520** or HD or PD or directly to patient **516** for PD. Element **572** can alternatively be or additionally include a filter, such as an ultrafilter to further clean the dialysate, e.g., so that the dialysate is close to or at an injectable quality level.

After leaving ED/EDI unit **530** via flow path **552**, one or more dialysis components from a concentrate metering source **548** via flow paths **582** may be introduced back into the cleaned dialysis fluid stream for mixing at reservoir **572**, e.g., via one or more pump **598c** and **598d** and associated valves. The mixing may also include purified water from source **592**. The concentrates in general include electrolytes and/or glucose/dextrose and are tailored for the specific type of dialysis performed. An additional purification or treatment component in the form of a filter or ultraviolet bactericidal light **574** can be added to recirculation circuit **514**. As is illustrated in FIG. 8, light **570** can be placed in dialysis circuit **514** as shown or blood or peritoneal dialysis treatment fluid can be directly subjected to bactericidal light **574** to enhance the bacterial purity of system **510**. The treated fluid (blood or dialysate) can then enter individual **516** via flow path **524**.

Circuits of the present disclosure may further include one or more conductivity sensor. Conductivity sensors may be placed at any suitable location along the fluid flow pathway. For example, and referring to the particular embodiment shown in FIG. 8, a conductivity sensor **596a** may be placed in fluid connection between EDI component **590** and ion exchange unit **560**, such that the conductivity of the dialysis fluid (and therefore the ion content of the fluid) exiting the EDI component **560** can be determined. Further or alternatively, a conductivity sensor **596b** can be placed in fluid connection between ion exchange unit **590** and dialysate reservoir **572** (when present) or dialyzer **520**. When dialysate reservoir **572** is present, a conductivity sensor **596c** may be in fluid connection between dialysate reservoir **572** and dialyzer **520**. Thus, in some embodiments, recirculation circuit **514** includes at least two of conductivity sensors **596a**, **596b**, and **596c**. In some embodiments, recirculation circuit **514** includes all three of conductivity sensors **596a**, **596b** and **596c**.

Conductivity sensors **596a** to **596c** are temperature compensated in one embodiment. The conductivity sensors in essence confirm that salt ions have been removed when desired (e.g., at sensor **596a**) and have in turn been added back into solution when desired (e.g., at sensors **596b** and **596c**). As discussed, system **510** and other systems of the present disclosure may further include one or more fluid pump for transporting spent dialysate, regenerated dialysate, reagent concentrates, water, or other fluids throughout the circuit. In some embodiments, for example the embodiment shown in FIG. 8, plural pumps **598a** to **598f** are used to transport various fluids. The pumps can be machine actuated fluid pumps. For example, embodiments in which pump dialysate reservoir **572** is used to hold regenerated dialysate, pump **598a** feeds regenerated dialysate to dialyzer **520**. Ultrapure or sterile water is likewise provided from ultrapure or sterile water source **592** to dialysate reservoir **572** via pump **598b** and to EDI component **590** via pump **598f**. And as discussed, acid concentrate and bicarbonate are provided from concentrate or fluid metering source **548** via pump **598c** and/or **598d**. Acid solution from acid source **594** is provided to ED component **580** via pump **598e**. Pumps **598a**

12

to **598f** can be membrane pumps, rotary peristaltic pumps, linear peristaltic pumps, shuttle pumps, or microfluidic pumps, which can be provided in any combination and hybridization to maximize performance and cost. Pumps **598a** to **598f** can have fluid contacting portions or chambers that are provided as part of a disposable cassette or be tubing portions that operate with tubing actuators.

Referring generally now to FIG. 9, a dialysis fluid system **610** for hemodialysis or peritoneal dialysis, having recycling capabilities, is shown in which water for regenerating dialysate is provided in part by a purified or sterile water source **692** and in part from tap water source **699**. Alternatively, tap water **699** is used as the sole source for regeneration water. In some embodiments, about six to twelve liters of ultrapure or sterile water per dialysis session are provided by purified or sterile water source **692** and the balance of water required to regenerate dialysate, e.g., up to eighteen total liters, is provided by tap water source **699**. Alternatively, all twelve to eighteen liters of regeneration water is tap water from source **699**.

As shown in FIG. 9, system **610** is otherwise very similar to or the same as system **510**. For example, a blood or peritoneal dialysis sterile fluid circuit **612** cycles fluid, e.g., blood or sterile peritoneal dialysis fluid, from an individual **616** through a dialyzer **620** and returns the fluid to the individual's body. A recirculation circuit **614** includes a combination ED/EDI unit or module **630** in the dialysis fluid recycling regime. As with system **510**, system **610** in a peritoneal dialysis application may provide the recirculation loop as a secondary loop using dialyzer **620** or provide the recirculation loop in a single loop arrangement, eliminating dialyzer **620** and merging circuits **612** and **614**. Here, dialysis fluid returning directly to the patient needs to be sterile or of injectable quality. The combination ED/EDI unit **630** includes an ED component **680** in fluid connection with an EDI component **690** via flow path **682**. ED/EDI unit or module **630** can be constructed and used once or reused as described above.

As with System **510**, ED component **680** can include a central chamber **683**, an anion chamber **684** having an anode **685**, and a cation chamber **686** having a cathode **687**. As fluid flows through central chamber **683** via flow path **684**, a potential difference between anode **685** and cathode **687** causes the electrolytes in the fluid in central chamber to flow or migrate into anion chamber **684** and cation chamber **686**. The treated fluid that passes through the ED component **680** enters the EDI component **690** via flow path **682**. A waste fluid stream filled with electrolytes exits via flow path **654** that leads to a drain **670**.

The EDI component **690** can again include a central chamber **632**, an anion chamber **634** having an anode **635**, and a cation chamber **636** having a cathode **637**. EDI component **690** is in fluid connection at junction **638** with an acid solution or acid concentrate **694** and sterile water source **692**. As spent dialysate flows through central chamber **632** via flow path **644**, a potential difference between anode **635** and cathode **637** causes the electrolytes in the fluid in central chamber to flow or migrate into anion chamber **634** and cation chamber **636**. The treated fluid that passes through the EDI component **690** exits as part of a treated fluid stream **652**.

The ED/EDI unit **630** can also be modified so that a suitable quantity of fluid can be recirculated around the ED/EDI unit **630** via flow paths **656** or via a single recirculation path **656** connected to both ED component **680** and EDI component **690**. Again, recirculation reduces the

13

amount of fluid flowing through ED/EDI unit **630** that would end up as part of the waste fluid stream discarded to drain **670**.

Recirculation circuit **614** can also include a carbon source **640** and a urease source **650** connected to carbon source **640** via flow path **642**. Circuit **614** can further include an optional ion exchange unit **660** in fluid connection with ED/EDI unit **630** via flow path **652**. Flow path **652** can lead directly back to dialyzer **620** or to a dialysate reservoir **672**. Carbon source **640**, urease source **650**, ion exchange unit **660**, and/or ED/EDI unit **630** can be in the form of removable cartridges. As with system **510**, carbon source **640** and urease source **650** receive spent fluid from dialyzer **620** and feed fluid to ED/EDI unit **630**. Carbon source **640** and urease **650** are alternatively downstream of ED/EDI unit **630**.

After leaving ED/EDI unit **630** via flow path **652**, one or more dialysis components from a concentrate or fluid metering source **648** via flow path **682** may be specifically tailored for the specific type of dialysis performed and mixed with purified water from source **692** in reservoir **672** if desired. An additional purification or treatment component in the form of a filter or ultraviolet bactericidal light **674** can be added to dialysis recirculation fluid circuit **614** as illustrated or alternatively to blood or patient circuit **612**. In the latter instance, when added to blood or patient circuit **612**, fluid exiting dialyzer **620** via flow path **624** can be further filtered or subject to a bactericidal light to enhance the bacterial purity of system **610**. The treated fluid can then enter individual **616** via flow path **624**.

System **610** may further include one or more conductivity sensor. Conductivity sensors may be placed at any suitable location along the fluid flow pathway to confirm that salt ions have been desirably removed or added as the case may be. For example, and referring to the particular embodiment shown in FIG. 9, a conductivity sensor **696a** can be in fluid connection between EDI component **690** and ion exchange unit **660**, such that the conductivity of the fluid (and therefore the ion content of the fluid) exiting the EDI component **690** can be determined. Alternatively or additionally, a conductivity sensor **696b** can be in fluid connection between ion exchange unit **690** and dialysate reservoir **672** (when present) or dialyzer **620**. When dialysate reservoir **672** is present, a conductivity sensor **696c** may be in fluid connection between dialysate reservoir **672** and dialyzer **620**. In some embodiments, the circuit **614** includes at least two conductivity sensors **696a**, **696b**, and **696c**. Thus in some embodiments, recirculation circuit **614** includes all three of conductivity sensors **696a**, **696b** and **696c**.

System **610** further includes one or more fluid pump for transporting spent dialysate, regenerated dialysate, reagent concentrates, water, or other fluids throughout the circuit. Each and every pump construction and positioning specification and alternative discussed above for system **510** is applicable to system **610**. In FIG. 9, pumps **698a** to **698f** are used to transport various fluids. In embodiments in which pump dialysate reservoir **672** is used to hold regenerated dialysate, pump **698a** feeds the regenerated dialysate from reservoir to dialyzer **620**. Reservoir **672** is alternatively a filter, such as an ultrafilter. Or, the filter can be provided in addition to reservoir **672**. In either case, the filter, e.g., ultrafilter, may bring the water or dialysis fluid close to or to injectable quality level. Ultrapure or sterile water is provided from sterile or ultrapure water source **692** to dialysate reservoir **672** via pump **698b** and to EDI component **690** via pump **698f**. Pump **698f** pumps tap water from tap **699** to EDI unit **690**. Acid concentrate and bicarbonate are provided from concentrate or fluid metering source **648** by pump **698c** and/or **698d**. Acid solution from acid source **694** is provided to EDI component **690** via pump **698e**. Pumps **698a** to **698f**

14

can be of any type described above and can be used if desired with a dialysis pumping cassette.

In addition to the modifications described herein, the dialysis fluid recycling systems can be further enhanced in several ways. First, the dialysis fluid recycling systems can remove nearly all solutes from the used or spent dialysis solution (including therapeutically beneficial solutes, which would then need to be re-added). The dialysis fluid recycling systems can also be designed to allow reduced removal of the active osmotic agent in the peritoneal dialysis fluid (e.g., glucose or dextrose). The osmotic reagent can be replaced with a longer acting molecule, such as glucose microspheres that can be reintroduced into the dialysis fluid, to maintain the osmotic gradient in the individual.

Apparatuses **730** and **830** of FIGS. 17A and 17B can be used in any type of blood dialysis treatment, e.g., hemodialysis ("HD"), hemofiltration ("HF"), or hemodiafiltration ("HDF"). Apparatuses **730** and **830** can also be used in any type of peritoneal dialysis ("PD") treatment, such as continuous cycling peritoneal dialysis ("CCPD") or tidal peritoneal dialysis. A combination ED/EDI apparatus is prepared by modifying a commercially available ED unit (e.g., ED200, PCCell) to reduce the width *W* by half and double the separation length *L*, and by modifying a single EDI unit (e.g., EDI15, Millipore) to reduce the thickness by half. FIG. 17A shows a combination ED/EDI apparatus **730** that is capable of removing 99.9% of ions when a 180 millimolar ("mM") spent dialysate stream is processed at 250 mL/min. The system **730** includes a single ED unit **780** in the illustrated embodiment, which is in fluid communication with a plurality (e.g., two, three, four or more) of EDI units **790**. ED unit **780** includes a central chamber **783**, a cation chamber **786** having a cathode **787**, and an anion chamber **784** having an anode **785**. Each EDI unit **790** includes a central chamber **732**, a cation chamber **736** having a cathode **737**, and an anion chamber **734** having an anode **735**. Each EDI unit **790** rejects a cation waste stream from the cation chamber **736** and an anion waste stream from the anion chamber **734**, which can be routed to drain **790**.

In the configuration shown in FIG. 17A, three EDI units **790** (e.g., each model EDI15, Millipore) are connected in parallel to one ED unit **780** (e.g., ED200, PCCell). In an example operation, a spent dialysate stream enters ED unit **780** via fluid path **701** at a flow rate of for example 250 mL/min. When operated at typical power levels (e.g., 130 watts), the treated fluid stream exiting ED unit **780** via flow path **782** has about 70% lower ion content than the spent dialysis stream (i.e., ED unit **780** removes about 70% of the ions from the spent dialysate stream). This partially treated fluid stream is then split and fed into three EDI units **790**, each operating at a typical power level of about forty watts. The treated streams exiting the EDI units **790** are combined in fluid path **752**, which has about 0.1% of the ion content of the original spent dialysate fluid stream (i.e., the combination ED unit **780** with the three EDI units **790** operating in parallel each at about forty watts removes about 99.9% of the ions remaining from the original spent dialysis stream). The total power consumption in this example is 130+40+40+40=250 watts, and the total ion removal is about 99.9%.

FIG. 17B shows another ED/EDI embodiment of the present disclosure. In comparison to apparatus **730** shown in FIG. 17A, apparatus **830** uses only a single modified EDI unit **890** which, in combination with a single modified ED unit **880**, is capable of removing at least about 99.9% of the ions from a 180 mM spent dialysate stream at a flow rate of 250 mL/min, and uses significantly less power (about 170 watts vs. about 250 watts).

In the embodiment shown in FIG. 17B, spent dialysate enters the modified ED unit **880** via fluid paths **801** and **802**, respectively. The modified ED unit **880** has in one embodi-

15

ment about twice the separation length L as ED unit **780** shown in FIG. 17A, and includes central chamber **883**, a cation chamber **886** having a cation **887**, and an anion chamber **884** having an anode **885**. The extended separation length L can be accomplished by any suitable method including, for example and without limitation, inclusion of additional flow channels (e.g., one or more flow barriers in the housing of the modified ED unit **880**) that forces the spent dialysate to travel farther through the modified ED unit **880** before exiting compared to a comparable, unmodified ED unit having a standard flow path length L. In one embodiment, modified ED unit **880** has an extended separation length L while having the same or essentially the same exterior dimensions as a comparable unmodified ED unit.

Due to the extended separation length L, modified ED unit **880** can achieve the same or better ion removal performance than commercially available ED unit **780** (e.g., at least about 85%, at least about 88%, or at least about 90%, etc., of the ions in the spent dialysate stream), while requiring less power input. For example, modified ED unit **880** can be operated at about 90% to 95%, e.g., about 92%, of its standard power level (e.g., at about 120 watts compared to PCCell ED200's standard power level of 130 watts). The resulting partially treated fluid stream exits the modified ED unit **880** via fluid path **882** and enters the modified EDI unit **890**, where it flows through central chamber **832** via flow path **844**.

Modified EDI unit **890** has a reduced thickness T compared to EDI unit **790**. The reduced thickness T can achieved

16

99.2%, or more particularly at least about 99.5%, or most particularly about 99.9%, of the ions in the spent dialysate stream.

In an example operation, blood or spent dialysate enters modified ED unit **880** via flow path **801**. Fluid streams **858** exiting cation chamber **886** and anion chamber **884** can be routed to drain (not shown) or recycled through the ED/EDI unit **830** in the same manner as shown in FIGS. 8 and 9. Fluid stream **882** exits the central chamber **883** of modified ED unit **880** and enters central chamber **832** of modified EDI unit **890** along flow path **844**. Fluid streams **856** exiting cation chamber **836** and anion chamber **834** can be routed to drain (not shown) or recycled through the ED/EDI unit **830** in the same manner as shown in FIGS. 8 and 9. Purified blood or dialysate exits modified EDI unit **890** via flow path **852** and is returned to the patient or dialyzer.

Combination ED/EDI unit **830** shown in FIG. 17B uses fewer EDI units (which are comparatively more expensive than ED units) and consumes less power than required by the comparable combination ED/EDI system or apparatus **730** shown in FIG. 17A. Thus, for a given flow rate, the cost and total power consumption of the combination modified ED unit/modified EDI apparatus **830** of the present disclosure are reduced, while achieving the same ion removal performance as apparatus **730** and other presently available ED units and EDI units. Comparative power consumption data required to achieve a total ion removal of 99.9% is provided in Tables 1A and 1B:

TABLE 1A

Power Consumption for Unmodified ED Unit with Three Unmodified EDI Units.							
Entry	Input solute conc.	Dialysate flow rate (mL/min)	ED Unit (1)		EDI Units (3)		Total Power
			Power	% Ion Removal	Power	% Ion Removal	
1A	140 mM	100	35 W	86%	22 W	99.3%	57 W
2A	180 mM	250	102 W	78%	66 W	99.5%	168 W

TABLE 1B

Power Consumption for Modified ED Unit with One Modified EDI Unit.							
Entry	Input solute conc.	Dialysate flow rate (mL/min)	Mod. ED Unit (1)		Mod. EDI Unit (1)		Total Power
			Power	% Ion Removal	Power	% Ion Removal	
1B	140 mM	100	38 W	94%	1 W	98.4%	39 W
2B	180 mM	250	115 W	88%	49 W	99.2%	164 W

by any suitable method including, for example, reducing the distance between membrane layers within the EDI unit. In one embodiment, modified EDI unit **890** has reduced distance between membrane layers while having the same or essentially the same external dimensions as a comparable unmodified EDI unit.

Modified EDI unit **890** includes a central chamber **832**, a cation chamber **836** having a cathode **837**, and an anion chamber **834** having an anode **835**. In one embodiment, modified EDI unit **890** is operated at an elevated power level compared to EDI unit **790** (e.g., about 105% to about 150%, or about 120% to 130%, or more particularly about 125% (about 50 watts) compared to Millipore's EDI15 power rating of 40 watts), such that the ED unit **880** and EDI unit **890** collectively remove at least about 99%, or at least about

Apparatuses **730** and **830** can be used with any of the systems discussed above, such as systems **10**, **110**, **210**, **310**, **410**, **510**, and/or **610**.

EXAMPLES

By way of example and not limitation, the following examples are illustrative of embodiments of the present disclosure.

Example 1

Experiments to determine the extent of the electrolyte removal using an EDI unit were performed. The experiments simulated EDI treatment of a post-urease dialysate. A peri-

toneal dialysis solution was spiked with 3200 ppm of Ammonium Carbonate (2000 ppm of urea can be converted into 3200 ppm of ammonium carbonate by urease). In different studies, the dialysis solution was passed through the EDI unit at a flow rate of 100 mL/min and 200 mL/min.

A Millipore EDI-15 Cell with a PK Precision VSP-12010 DC power supply was used as the EDI unit. Conductivity of the dialysis solution was measured using an Amber Science EC3084 Conductivity Meter.

During the experiments, the conductivity of the treated dialysis solution versus corresponding voltage/current of the EDI unit was measured. The final conductivity was compared to the original conductivity of the untreated dialysis solution. A summary of the results is shown in Table 2 and FIGS. 6 and 7. FIG. 6 shows the conductivity of a dialysis solution treated using the EDI unit versus the operating voltage of the EDI unit. FIG. 7 shows the operating current of the EDI unit versus the operating voltage of the EDI unit.

TABLE 2

Dialysate flow rate (mL/min)	Voltage (Volts)	Current (Ampere)	Conductivity (mS/cm)	% Removal
100	0	0	15.9	0
100	20	2.1	8.4	47
100	40	3.6	2.28	86
100	60	4.3	0.48	97
100	80	5.6	0.08	99
200	80	8.6	0.44	97

As shown in Table 2 and FIGS. 6 and 7, a 99% electrolyte removal from the dialysis solution can be achieved using the EDI unit. It was also found that the EDI unit can be operated at a reduced voltage and reduced current to allow a specific percentage of electrolytes to pass through. This could allow the use of a smaller size EDI unit for better portability. In this case, the small amount of residue electrolytes, including ammonium ions, can be removed by a supplemental ion-exchange resin column down stream from the EDI unit.

Example 2

Experiments to determine the extent of the electrolyte removal using an ED unit of the present disclosure were performed. The experiments simulated ED treatment of a post-urease dialysate. A peritoneal dialysis solution (Accusol 35, Baxter Healthcare) was spiked with Ammonium Carbonate (5 mM) and passed through the ED unit at 45 volts and at a flow rate of about twenty to about 340 mL/min. The electrolyte concentration was analyzed using an Olympus AU400e Clinical Analyzer. The percentage of each ion removed was determined by comparing it with the concentration of the solution entering the EDI unit. Cation removal preference as a function of dilute-in flow rate is shown in FIG. 10 for sodium, ammonium, potassium, calcium and magnesium. In general, the ED/EDI unit preferentially removed magnesium over calcium over sodium over potassium over ammonium cations under these conditions. Anion removal preference as a function of dilute-in flow rate for the same system is shown in FIG. 11 for bicarbonate and chloride anions, with chloride being removed more preferentially than bicarbonate.

The corresponding power consumption of the EDI unit at these data points on shown on FIG. 10 and FIG. 11 is plotted in FIG. 12. As shown in FIG. 12, less than 150 watts is required to remove greater than 80% of the ammonium cations at a dialysate flow rate of less than 300 mL/min.

Example 3

Experiments to determine the extent of the electrolyte removal using an EDI unit were performed. The experiments simulated EDI treatment of a post-urease dialysate. A peritoneal dialysis solution (Accusol 35, Baxter Healthcare) was passed through the EDI unit at flow rates of eighty-nine mL/min and forty-seven mL/min. The electrolyte concentration was analyzed using an Olympus AU400e Clinical Analyzer. The percentage of each ion removed was determined by comparing it with the concentration of the solution entering the EDI unit.

FIG. 13 shows relative removal rates for calcium compared to sodium. At both forty-seven and eighty-nine mL/min flow rates, calcium cations were removed at a faster rate than sodium cations were removed. For example, at forty-seven mL/min, less than 20% of the sodium cations had been removed by the time the calcium cations were nearly completely removed from the dialysate solution. Results were qualitatively similar at a flow rate of eighty-nine mL/min. This data indicates that EDI preferentially removes calcium cations over sodium cations.

FIG. 14 shows relative removal rates for magnesium and sodium cations at forty-seven and eighty-nine mL/min. At both forty-seven and eighty-nine mL/min flow rates, magnesium cations were removed at a faster rate than sodium cations were removed. For example, at forty-seven mL/min, less than 20% of the sodium cations had been removed by the time the magnesium cations were nearly completely removed from the dialysate solution. Results were qualitatively similar at a flow rate of eighty-nine mL/min. This data indicates that EDI preferentially removes magnesium cations over sodium cations.

Example 4

Experiments to determine the extent of the electrolyte removal using an EDI unit were performed. The experiments simulated EDI treatment of a post-urease dialysate. A peritoneal dialysis solution having 140 Mm sodium chloride and thirty Mm ammonium carbonate was prepared (an initial molar ratio of $\text{Na}^+/\text{NH}_4^+$ of about 2.3:1 was passed through the EDI unit at flow rates of one-hundred mL/min and ninety-seven mL/min under different applied electric current conditions to achieve different levels of ion removal by the EDI unit. The electrolyte concentrations of the fluid entering the EDI unit and the effluent fluid from the EDI unit were analyzed using an Olympus AU400e Clinical Analyzer. The molar ratio of $\text{Na}^+/\text{NH}_4^+$ in the effluent fluid from the EDI unit is compared with the molar ratio of $\text{Na}^+/\text{NH}_4^+$ in the incoming fluid. An increase of the $\text{Na}^+/\text{NH}_4^+$ molar ratio will indicate a preference of removing NH_4^+ ion over Na^+ by the EDI unit.

FIG. 15 shows the relative removal rates for sodium and ammonium cations at different levels of ion removal. In this experiment, the simulated dialysate was passed through the EDI unit at flow rates of one-hundred mL/min and ninety-seven mL/min. At each flow rate and across the range of different ion removal, the sodium/ammonium molar ratio increased slightly over the incoming fluid, indicating that the EDI removed slightly more ammonium cations than sodium ions at both flow rates.

FIG. 16 shows relative removal rates for chloride and bicarbonate anions when the same dialysate solution used to generate FIG. 15 was passed through the EDI unit at flow rates of one-hundred mL/min and ninety-seven mL/min. The initial $\text{Cl}^-/\text{HCO}_3^-$ ratio was about 4.7:1 in the incoming

fluid, and decreased over the range of different levels of ion removal and at both flow rates. A decrease of the $\text{Cl}^-/\text{HCO}_3^-$ molar ratio in the effluent fluid in comparison with the incoming fluid will indicate a preference of removing Cl^- ion over HCO_3^- by the EDI unit. This data indicates that EDI removes chloride anions at a faster rate than bicarbonate anions.

Aspects of the Present Disclosure

Aspects of the subject matter described herein may be useful alone or in combination one or more other aspect described herein. Without limiting the foregoing description, in a first aspect of the present disclosure, a dialysis fluid system recycling used dialysis fluid comprises a carbon source, a urease source in fluid communication with the carbon source, and an electrodialysis/electrodeionization (“ED/EDI”) unit in fluid communication with at least one of the carbon and urease sources, the ED/EDI unit including an ED component, and an EDI component in fluid communication with the ED component.

In accordance with a second aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the dialysis fluid system includes an ion exchange unit operating with the ED/EDI unit to recycle used dialysis fluid.

In accordance with a third aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the dialysis fluid system includes a concentrate metering source located downstream of the ED/EDI unit.

In accordance with a fourth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, at least a portion of fluid within the ED/EDI unit of the dialysis fluid system is recirculated back into the ED/EDI unit.

In accordance with a fifth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the ED unit includes multiple ED units.

In accordance with a sixth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, a hemodialysis system recycling used dialysis fluid comprises a blood circuit and a dialysis fluid circuit in fluid communication with a dialyzer, a carbon source in the dialysis fluid circuit, a urease source in fluid communication with the carbon source, and an electrodialysis/electrodeionization (“ED/EDI”) unit in fluid communication with at least one of the carbon and urease sources and, the ED/EDI unit including an ED component and an EDI component in fluid communication with the ED component.

In accordance with a seventh aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the hemodialysis system includes an ion exchange unit in the dialysis fluid circuit.

In accordance with an eighth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the hemodialysis system includes a concentrate metering source located downstream of the ED/EDI unit.

In accordance with a ninth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the hemodialysis system includes a filter in the dialysis fluid circuit.

In accordance with a tenth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the hemodialysis system includes an ultra-

violet bactericidal light positioned and arranged to irradiate at least a portion of the blood circuit or the dialysis fluid circuit.

In accordance with an eleventh aspect of the present disclosure, which may be used with any one or more aspect discussed herein, a peritoneal dialysis system comprises a dialysis fluid recirculation flow path configured to be placed in fluid communication with the peritoneal cavity of a patient, a carbon source in the dialysis fluid recirculation flow path, a urease source in fluid communication with the carbon source, and an electrodialyzer/electrodeionization (“ED/EDI”) unit in fluid communication with one of the carbon and urease sources, the ED/EDI unit including an ED component, and an EDI component in fluid communication with the ED component.

In accordance with a twelfth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the peritoneal dialysis system includes an ion exchange unit in the dialysis fluid recirculation flow path.

In accordance with a thirteenth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the peritoneal dialysis system includes a concentrate metering source located downstream of the ED/EDI unit.

In accordance with a fourteenth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the dialysis fluid recirculation flow path of the peritoneal dialysis system runs from the patient or a dialyzer, through the carbon source, the urease source and the ED/EDI unit, in any order, back to the patient or the dialyzer.

In accordance with a fifteenth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the peritoneal dialysis system includes an ultraviolet bactericidal light positioned and arranged to irradiate at least a portion of the dialysis fluid recirculation flow path.

In accordance with a sixteenth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, a method of performing hemodialysis comprises passing dialysis fluid from a dialyzer through, in any order, a carbon source, a urease source, an electrodialysis (“ED”) component, and an electrodeionization (“EDI”) component to produce a cleaned dialysis fluid, and returning the cleaned dialysis fluid to the dialyzer.

In accordance with a seventeenth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the method includes passing the dialysis fluid through an ion exchange unit before returning the cleaned dialysis fluid to the dialyzer.

In accordance with an eighteenth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the method includes adding at least one dialysis fluid concentrate to the dialysis fluid before returning the cleaned dialysis fluid to the dialyzer.

In accordance with a nineteenth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the method includes draining a portion of the dialysis fluid that is passed through at least one of the ED and EDI components.

In accordance with a twentieth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the method includes recirculating a portion of the dialysis fluid that is passed through at least one of the ED and EDI components.

21

In accordance with a twenty-first aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the method includes adding at least one of sterile/injectable or tap water to the dialysis fluid.

In accordance with a twenty-second aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the method includes filtering the dialysis fluid before returning the cleaned dialysis fluid to the dialyzer.

In accordance with a twenty-third aspect of the present disclosure, which may be used with any one or more aspect discussed herein, a method of performing peritoneal dialysis comprises recirculating dialysis fluid removed from a patient or dialysate through, in any order, a carbon source, a urease source, an electro dialysis (“ED”) component, and an electrodeionization (“EDI”) component to produce a cleaned dialysis fluid, and returning the cleaned dialysis fluid to the patient or dialyzer.

In accordance with a twenty-fourth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the method includes passing the dialysis fluid through an ion exchange unit before returning the cleaned dialysis fluid to the patient.

In accordance with a twenty-fifth aspect of the present disclosure, which may be used with any one or more aspect discussed herein, the method includes adding at least one dialysis fluid concentrate to the dialysis fluid before returning the cleaned dialysis fluid to the patient.

In accordance with a twenty-sixth aspect of the present disclosure, any of the structure, functionality and alternatives illustrated and described in connection with any combination of one, or more, or all of FIGS. 1 to 17B may be used in combination with any one, or more, or all of the preceding aspects.

It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present subject matter and without diminishing its intended advantages. It is therefore intended that such changes and modifications be covered by the appended claims.

The invention is claimed as follows:

1. A method of performing hemodialysis comprising: passing dialysis fluid from a dialyzer through, in any order, a carbon source, a urease source, and a combi-

22

nation unit comprising an electro dialysis (“ED”) component and an electrodeionization (“EDI”) component to produce a cleaned dialysis fluid, wherein the ED component and the EDI component are separate, and wherein the dialysis fluid is passed within the combination unit via a fluid path from the ED component to the separate EDI component; and

returning the cleaned dialysis fluid to the dialyzer.

2. The method of claim 1, which includes passing the dialysis fluid through an ion exchange unit before returning the cleaned dialysis fluid to the dialyzer.

3. The method of claim 1, which includes adding at least one dialysis fluid concentrate to the dialysis fluid before returning the cleaned dialysis fluid to the dialyzer.

4. The method of claim 1, which includes draining a portion of the dialysis fluid that is passed through at least one of the ED and EDI components.

5. The method of claim 1, which includes recirculating a portion of the dialysis fluid that is passed through at least one of the ED and EDI components.

6. The method of claim 1, which includes adding at least one of sterile/injectable or tap water to the dialysis fluid.

7. The method of claim 1, which includes filtering the dialysis fluid before returning the cleaned dialysis fluid to the dialyzer.

8. A method of performing peritoneal dialysis comprising: recirculating dialysis fluid removed from a patient or dialyzer through, in any order, a carbon source, a urease source, and a combination unit comprising an electro dialysis (“ED”) component and an electrodeionization (“EDI”) component to produce a cleaned dialysis fluid, wherein the ED component and the EDI component are separate, and wherein the dialysis fluid is passed within the combination unit via a fluid path from the ED component to the separate EDI component; and

returning the cleaned dialysis fluid to the patient or dialyzer.

9. The method of claim 8, which includes passing the dialysis fluid through an ion exchange unit before returning the cleaned dialysis fluid to the patient.

10. The method of claim 8, which includes adding at least one dialysis fluid concentrate to the dialysis fluid before returning the cleaned dialysis fluid to the patient.

* * * * *